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THE AETIOLOGY OF CHRONIC NEPHRITIS IN QUEENSLAND.

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AN investigation of chronic nephritis in Queensland was carried out during the years 1951 to 1955. Three papers, dealing respectively with a follow-up of cases of plumbism in childhood (Henderson, 1954), mortality data (Henderson, 1955), and lead content of bone in chronic renal disease (Henderson and Inglis, 1957), have been published, and another paper is in preparation describing the clinical and pathological features of the chronic renal lesion due to lead. The purpose of the present paper is to summarize and collate the several lines of evidence which have led to the conclusion that plumbism in childhood was solely responsible for an unusually high incidence of chronic nephritis in this State.

HISTORICAL REVIEW.

The first mention in the literature of a particular problem in relation to chronic nephritis in Queensland was in 1897. Halford, in discussing papers on lead poisoning in childhood delivered at a meeting of the British Medical Association, observed that granular contracted kidneys in persons under 30 years of age were more frequent in

Brisbane than in the southern capital cities of Australia. Although practitioners were, no doubt, aware of the prevalence of the disease, nothing further was published until 1917, when Mathewson commented on a paper by Gibson on "Plumbic Ocular-Neuritis". He stated that the mortality in Queensland from chronic nephritis was, in the 15 to 20 years age group nine times, in the 20 to 25 years age group five to seven times, and in the 25 to 30 years age group nine times that in Sydney, and related it to the high incidence of lead poisoning in Queensland children. There was no mention of the source of his figures.

In 1922, in an historical account of lead poisoning in Queensland children, the Council of the Queensland Branch of the British Medical Association made the statement:

There is a strong impression among some Brisbane practitioners that the prevalence of chronic nephritis among young adults in this city is partly a late result of the absorption of lead during childhood.

The first detailed comparison of Queensland mortality from the disease with that elsewhere was made by Croll in 1929. His statistics were taken from the records of the Registrar-General for the ten-year period, 1917 to 1926. He estimated that, during those 10 years, 884 persons aged under 40 years died in Queensland from chronic nephritis due to some factor which was not operating in the other States.

At the same time, Nye (1929) published the first serious attempt to elucidate the aetiology of the disease. He described the clinical features, and presented evidence to

show that there was a close association between the chronic nephritis of Queensland and lead poisoning in childhood.

As a result of this article, the Queensland Branch of the British Medical Association wrote to the Commonwealth Department of Health, stressing the gravity of the problem and recommending a comprehensive inquiry. R. W. Cilento was appointed to conduct the inquiry. He was unable to complete it, and an Interim Report was presented in 1932 (Cilento, 1932). In the statistical section, Cilento made use of the Registrar-General's mortality figures from 1907 to 1931 to show that the death rate from chronic nephritis under the age of 40 years was very high in Queensland throughout this period, and it was increasing. His tentative conclusions on aetiology were that lead poisoning in childhood, in conjunction with a number of other factors, appeared to be partly responsible for the chronic nephritis in young people in Queensland. The report stressed the possibility that undiagnosed scarlet fever might be an important aetiological agent.

In 1933, Nye criticized the Interim Report, minimizing the importance of scarlet fever, and giving additional evidence in support of his thesis that lead poisoning in childhood was the major cause.

At the request of the Queensland Government, the Walter and Eliza Hall Institute of Research in Pathology and Medicine assigned K. Fairley to review the whole of the evidence on chronic nephritis in Queensland. He (Fairley, 1934) concluded that lead poisoning in childhood accounted for part of the chronic nephritis in Queensland, but that further work was necessary to determine the magnitude of this part. As a result, R. E. Murray resumed the inquiry by the Commonwealth Department of Health which Cilento had been unable to complete in 1932. The work was interrupted again, and a report of the investigation as far as it went appeared in 1939 (Murray, 1939). *Inter alia* the following statements were made in the conclusions:

Chronic nephritis is unduly prevalent among young people in Queensland. At the present time, about 90 people below the age of thirty years, and approximately the same number between the ages of thirty and fifty years, die annually in excess of the number that would succumb to the disease were the death rates the same as those of England and Wales.

The evidence suggests that lead poisoning in childhood is a major factor in the causation of the abnormal Queensland incidence of chronic nephritis. Although it would appear that it is the sole factor responsible, it cannot be stated dogmatically that such is the case.

No further inquiries were made until the present investigation was begun in 1951.

The evidence to be presented here has been grouped in the following categories: (1) The mortality data. (2) Clinico-pathological analysis. (These show that the problem is a real one, and that it is due to a recognizable entity.) (3) Childhood plumbism as the causative agent: (a) previous investigations; (b) correlation of childhood plumbism with mortality data; (c) follow-up of childhood plumbism; (d) past history of patients with chronic renal disease; (e) analysis of familial incidence; (f) study of lead content of bone. (These all point to lead as the cause of the particular type of chronic renal disease with which we are concerned.) (4) The possibility that other causative agents may have operated, but may have been masked by an apparent correlation with lead; (5) the relation of lead poisoning to renal disease outside Queensland. (These two last categories are necessary as a check on the previous findings.)

MORTALITY DATA.

Mortality data provide a general picture of the problem, and indicate some of the qualities of the aetiological agent. Figure 1 shows the specific ten-year age group average annual death rates per 100,000 from chronic nephritis for ten-year periods during the years 1875 to 1949, in Queensland and the other States of Australia. The method of classification used by statistical departments throughout Australia was changed in 1950, so the figures for succeeding years are no longer comparable with those before. The age groups have been separated for clarity. Rates for 1947 are an average of four years only.

At this stage, it is desirable to emphasize that the term "chronic nephritis" used by the statistician in mortality statistics implies no single aetiological or pathological entity. It is merely a convenient label for a group of terms used by practitioners in certifying the cause of death. The terms classified as "chronic nephritis" are given in the International List of Causes of Death.

Other States of Australia.

The general picture is the same for both sexes, and the rates increase progressively with age. In the groups of age less than 60 years there is an irregular rise to a peak in about 1901, followed by a gradual fall until 1947. In the oldest groups, the rate rises until the period from 1931 to 1941. Rates for males and females are much the same in each age group, except that they are higher for males in the two oldest groups.

Queensland.

The Queensland graphs are quite different. The male and female rates are similar, although the female rates are slightly higher in the younger, and the males in the older, age groups. The female graphs will be discussed as representative of both sexes. In the 10 to 19 years group, there is a gradual rise to a peak in 1931, when the rate was 16.9 compared with 3.1 in the other States. This rise represents approximately 12 deaths annually in excess of those which would have occurred in Queensland if its rate had been the same as in the other States. After 1931, the rate falls to 3.5 in 1947. The 20 to 29 years group reaches a peak rate of 51.5 in 1931, compared with 7.6 in the other States—an annual excess in Queensland of approximately 32 deaths. In the 30 to 39 years group, the 1931 rate was 52.3 in Queensland and 19.1 in the other States, giving an annual excess of about 21 deaths. The peak rate in the 40 to 49 years group was 64.8, representing 13 extra deaths in Queensland above the rate in the other States of 39.1. In the 50 to 59 years age group, the 1931 rate was 79.5 in Queensland and 61.4 in the other States, giving about four extra deaths per year. Thus, during the period 1926 to 1935, there was, among the female population of Queensland aged from 10 to 59 years, an annual excess of 82 deaths, or 27 per 100,000 population of this age, over those which would have occurred at the same rate as in the other States. Similar but slightly lower figures apply to males. In the oldest age groups, the death rates show the same general pattern as in the other States, but at a consistently lower level.

It will be noted that there has been a decline in mortality in Queensland in recent decades. The decline is better illustrated in the female graphs (Figure 1). It begins after 1931 in the 10 to 19 years age group, and affects both the 20 to 29 years group and, to a lesser extent, the 30 to 39 years group after 1941. In the male graphs (Figure 1), the decline affected the 10 to 19 years group after 1931 and the 20 to 29 years group after 1941. It had not reached the 30 to 39 group in 1947. The reality of this decline has already been demonstrated (Henderson, 1955).

Queensland Mortality Compared with that of Other States.

The mortality from chronic nephritis in the other States of Australia is similar to that in New Zealand, and in England and Wales, and may be taken as the normal mortality from this cause. Some very interesting deductions can be made on comparing the normal mortality with Queensland mortality.

Let us consider when Queensland mortality first exceeded normal figures in the different age groups. This will be taken as the year in which the Queensland graphs cross those of the other States. Such crossing points, though not absolutely accurate, are adequate for purposes of comparison. In both males and females, the rates in the year 1881 will be ignored.

In females, the Queensland line crosses normal in the 10 to 19 years age group in 1895, in the 20 to 29 years groups in 1897, in the 30 to 39 years group in 1903, in the 40 to 49 years groups in 1915 and in the 50 to 59 years group in 1926. It does not cross normal or show any tendency to do so in the 60 to 69 or 70 to 100 years groups. The crossing

points are connected by the thin line in Figure 1. In males, the crossing points occur in 1891, 1896, 1909, 1923 and 1936 in the successive age groups up to 60 years, and, as in females, the graphs show no tendency to cross in the ages over 60 years. Thus the increased mortality in Queensland affected each age group up to 59 years at successively later dates, and examination of the intervals between these dates shows that, within the limitations of statistics of this type, their average approximates to 10 years.

This picture can be explained in only one way—that is, by an aetiological agent beginning to act on the children in Queensland in the period about 1880, and producing the death from chronic nephritis of different individuals aged from 10 to 40 years. The children affected between 1880 and 1890 would die when they were 10 years older and forming the 10 to 19 years group; more of these would die 10 years later when they were in the 20 to 29 years group, and so on until the deaths occurring, say, 45 years after the agent had acted on the children would raise the death rate in the 50 to 59 years age group about 1930. The continued action of the aetiological agent would maintain the high death rates in successive age groups, as each 10 year "batch" or "cohort" of individuals became 10 years older.

If such an agent ceased to act, then the fall in mortality should commence in the youngest group and pass successively into the older groups, finally reaching the 50 to 59 years group some 50 years later. It will be noted that the decline in mortality which has begun in Queensland is following such a pattern.

The beginning of the decline in the 10 to 19 years group after 1931 indicates that the agent acted on many fewer children between 1920 and 1930. The continuing high mortality in this group after 1941 shows that the disappearance of the noxious factor was gradual. It may be expected that mortality will fall in each age group in turn, until it finally returns to normal in the 50 to 59 years group in about 1990 to 2000. Then, provided that the agent has not reappeared in the meantime, all the individuals affected by it will have died, and the excess mortality from chronic nephritis in Queensland will cease to exist.

Summary.

On the basis of mortality data between 1876 and 1947, the excess mortality from "chronic nephritis" in Queensland is best explained by the action of a nephrotoxic agent on the children of Queensland. Such an agent would have commenced acting about 1880, initiating changes in the kidney leading to death from chronic renal disease 10 to 40 years later, and gradually ceased to act after 1920.

CLINICO-PATHOLOGICAL ANALYSIS.

The Sample.

Detailed analysis of a sample of chronic renal disease in this State was obviously necessary, in order to determine what type of disease has been raising the mortality in Queensland, and to obtain evidence of its aetiology. The sample was obtained by collecting patients who had suffered from chronic renal disease and who were examined at routine autopsy in Brisbane during the three and a half years between 1951 and 1955. Those who died in the 20 to 49 years age group were used for analysis, as the excess mortality occurred chiefly in this group. A total of 67 patients from whom histological sections were available were used for full examination. These represented about 12% of the 550 deaths that were classified as due to chronic nephritis in this age group in the State. Brisbane, where all those in the sample died, has been shown to contribute its share to the excess mortality in the whole State (Henderson, 1955). Table I shows the age and sex distribution of all Queensland deaths from "chronic nephritis", "hypertension with, and without, heart disease" and "infections of the kidney", which cover most deaths due to chronic renal disease, in comparison with those of the present sample. It is evident that these 67 cases can be taken as representing a random sample of chronic renal disease in the 20 to 49 years age group in Queensland.

Method.

Separate clinical and pathological diagnoses were made by myself and by Dr. J. A. Inglis, chief lecturer at the Department of Pathology, University of Queensland, respectively. Final diagnosis was reached by discussion. Approximately half of the patients were examined by me during life, and routine hospital records were used for most of the others. Cases were finally diagnosed as chronic glomerulonephritis, as chronic pyelonephritis, as primary hypertension, or as of "undetermined" aetiology.

As the mortality data showed that the cause operated in childhood, it was necessary to classify patients according to place of residence in childhood. This was done, as already discussed (Henderson and Inglis, 1957), by using place of birth. Seven of the total of 67 were born outside Queensland.

Results.

Of those born in Queensland, 12 patients could be allotted to generally accepted aetiological groups; five were diagnosed as suffering from chronic glomerulonephritis, three from chronic pyelonephritis and four from hypertension. Criteria of diagnosis have been discussed in an earlier paper (Henderson and Inglis, 1957). Forty-seven illnesses were recorded as being of "undetermined" cause, and one was considered separately because the renal contraction was unilateral, whereas the severity of the disease was approximately equal in the two kidneys in the remainder.

The clinical and histological features of the group of cases of undetermined aetiology will be described in detail in later paper. Clinically, they could only be labelled "renal failure with hypertension". No patient had a history of acute nephritis, of long-standing urinary infection, or of edema prior to terminal cardiac failure. The clinical and microscopic urinary findings provided no indication of aetiology. An interesting feature was the occurrence of gout in five males and three females in the absence of a family history of the disease. The gout was obviously not the cause of the renal disease, and its appearance in this series recalls the "saturnine gout" of earlier writers.

Macroscopically, the kidneys were contracted, with granular surfaces, and without the coarse lobulation of chronic pyelonephritis. The mean weights of the kidneys in the group were: right 77 grammes; left 76 grammes.

Histologically, proliferations of capsular epithelium and adhesions of glomerular tuft to capsule were observed in some cases. Usually these changes were recent and of minor importance so they were considered to be incidental, and not related to the cause of the long-standing contraction and fibrosis or to the long-standing clinical disease. In a few patients with severely contracted kidneys, these lesions were of sufficient severity and duration to suggest a histological diagnosis of chronic glomerulonephritis. However, indisputable histological evidence was lacking, and the diagnosis was not supported by the clinical history. After a survey of the whole series, it was clear that these cases were properly placed with cases of unidentified origin and not with those of glomerulonephritic origin. In some other cases the histological findings resembled those of hypertensive nephrosclerosis; but the kidneys of these patients showed unusually severe contraction, while clinically there was evidence of long-standing renal disease without severe hypertension. The general histological picture in the group is one of marked disappearance of renal tissue without indication of cause, changes such as those mentioned above being superimposed on the remaining parenchyma.

Such was the type of chronic renal disease predominating in this sample collected between 1951 and 1955. To find out if the same type predominated when mortality was at its maximum, the clinical records of all deaths of patients aged 20 to 39 years, classified as due to chronic nephritis at the Brisbane General Hospital during the years 1929 to 1933, were examined. The hospital used the same system of classification as the Registrar-General, so all these deaths would be included in the mortality data. There were 117 deaths, approximately 15% of the total Queensland mortality for the age group in the period. Their age and sex distributions are shown in Table I. The greater incidence of the disease in the younger patients at that

period, as compared with the present, is well demonstrated. The information provided by the records consisted of routine clinical data and macroscopic autopsy findings in 27 cases. It was impossible to make an accurate clinicopathological analysis, but it was clear that the general clinical picture of chronic renal disease in 1930 was the same as that in the present sample. The publications of Cilento (1932) and Nye (1933) contain further clinical descriptions which confirm this.

TABLE I.

Age and Sex Distribution of (a) All Deaths from Chronic Nephritis at Ages 30 to 59 Years at Brisbane General Hospital during the Years 1928 to 1933, (b) All Deaths from Chronic Renal Disease at Ages 20 to 49 Years throughout Queensland during the Years 1951 to 1955, (c) Deaths from Chronic Renal Disease Found at Autopsy in Brisbane during the Years 1951 to 1955.

Age Group, (Years.)	Hospital Deaths, 1928 to 1933.		All Queensland Deaths, 1951 to 1955.		Autopsy Series, 1951 to 1955.	
	Males.	Females.	Males.	Females.	Males.	Females.
20 to 24	17	15	12	15	2	0
25 to 29	14	16	16	20	6	4
30 to 34	10	15	44	38	7	5
35 to 39	14	16	51	78	11	9
40 to 44	—	—	65	82	7	9
45 to 49	—	—	69	68	6	8
Total	55	62	257	301	39	25

Summary.

Clinico-pathological analysis of a sample of chronic renal disease in the 20 to 59 years age group in Queensland showed that only small proportion of illnesses are due to generally recognized causes such as glomerulonephritis, pyelonephritis or hypertension. The majority of cases which produce the excess mortality in Queensland do not present the features of these diseases, and are due to some other cause.

LEAD POISONING IN CHILDHOOD AS THE CAUSE OF CHRONIC RENAL DISEASE IN QUEENSLAND.

Previous Investigations.

Henderson (1954) gave a brief historical account of lead poisoning in Queensland children. Gibson (1904) first investigated it and named weathered paint on Queensland houses as the source. As has been mentioned above, lead poisoning in childhood has long been regarded by local practitioners as the cause of the high incidence of chronic renal disease. Prior to the appearance of Nye's paper in 1929, this opinion had been based on clinical impression. Nye published the results of his investigation in a series of papers and finally in a monograph (Nye, 1929, 1930, 1933). His positive evidence, finally stated in the monograph, relating plumbism and chronic nephritis was essentially as follows. Of 186 patients suffering from "chronic nephritis" collected over six years, 33 gave a history of having been treated for plumbism in childhood. Only two patients had a history of acute nephritis and haematuria. Nye also studied 34 patients who had suffered severely from plumbism with paralysis in childhood some years previously. Of this study he states:

In seven instances no albumin was present in the urine; but the results of the renal function test revealed the appalling fact that of these thirty-four unfortunate young people, twenty-nine had renal insufficiency well established. In most cases, raised blood pressure, marked urea retention and low urinary concentration, indicated that sclerosis had already commenced.

From the description given, none of the patients had had a history of acute nephritis or oedema, and there was no microscopically evident haematuria or pyuria.

Nye also suggests that plumbism in childhood, of a degree insufficient to produce symptoms, might result in renal disease in later life. Of the observed familial incidence of chronic renal disease in Queensland, he states:

It is my belief that the familial or inborn habit of nail-biting and familial susceptibility to plumbism as previously discussed, are the factors responsible for the familial incidence of the disease in Queensland.

Apart from a general statement on histology, he gives no autopsy data.

Cilento (1933), in his Federal Report, described a study of 123 cases of chronic renal disease in Queensland. Thirty of these patients had a history of "definite" and 16 of "indefinite" plumbism in childhood; seven had a history consistent with an attack of acute nephritis. He stressed the occurrence of the disease in several siblings in a number of families. In a follow-up investigation of 28 individuals, who had been inmates of the Hospital for Sick Children with a diagnosis of plumbism based on the presence of paralysis with other symptoms of the disease, it was found that 19 had developed signs of chronic renal disease. No autopsy data are given.

Murray (1939) found a past history of plumbism in 18 of 55 cases of "chronic nephritis" in Queensland. He investigated 38 cases of plumbism of a somewhat milder degree than Cilento's cases, and found evidence of kidney involvement in 14. He also estimated the lead content of rib in 17 subjects of "chronic nephritis" who came to autopsy, and found it in all cases to be more than double the maximum normal figure of 1.75 milligrammes per 100 grammes recorded by Tompsett (1936).

These facts, in conjunction with opinion in the older literature that lead poisoning causes renal disease, led the above-mentioned writers to the conclusion that at least some of the "chronic nephritis" of Queensland was due to plumbism. All investigators were unable to ascribe the major part of the excess mortality to it, because only a third of their cases, at most, could be linked with lead poisoning by the only means available—a history of clinical plumbism. All agreed on the possibility of sub-clinical plumbism being responsible for the rest, but had no evidence to prove it.

Mortality Data.

The mortality data (Figure I) require that the aetiological agent responsible for the excess mortality from chronic nephritis in Queensland should have acted on children. It should have begun to act about 1880 and have diminished during the period 1920 to 1930. It should have produced death in from 10 to 40 years after its initial action.

Plumbism occurred in children in Queensland. The exact date of its appearance in the community cannot be determined. Turner (1892) was the first to diagnose a case in 1890, but the disease may have been in existence before that date. Weathered lead paint on the verandas of the type of house peculiar to Queensland has been shown to be the main source of the poison. It has been impossible to determine when lead paint was first used in this State, but old photographs of Brisbane show the erection of an increasing number of this particular type of house after about 1870. By 1893, when the great flood was a photographic event, they appear to form the majority of dwellings in the city. Thus, what evidence exists is consistent with the commencement of plumbism in Queensland about the time required by the mortality data.

The number of patients admitted to the Hospital for Sick Children provides a measure of the incidence of plumbism. Cilento (1932) states that there were 160 admissions, including re-admissions, between 1891 and 1915, but detailed figures are available only since 1915. New admissions are shown in Table II, and sporadic cases have occurred since 1935. The marked decline in new cases between 1925 and 1935, the time required by the mortality data, is obvious. This decline followed the introduction, in 1922, of legislation banning lead paint on surfaces accessible to children, and other factors which are discussed by Nye (1933).

The follow-up investigation, summarized below, showed deaths from chronic nephritis occurring five to 34 years after childhood plumbism. Plumbism in childhood as the aetiological agent of "chronic nephritis" in Queensland fulfils all the requirements imposed by mortality data.

Follow-up of Cases of Childhood Plumbism.

In the present study, a follow-up investigation of a large group of patients who had suffered from childhood plumbism was carried out. It has been described in detail previously (Henderson, 1954), and the results will be summarized. The group comprised 401 children admitted to the Hospital for Sick Children, Brisbane, between 1915 and 1935, with a diagnosis of lead poisoning. There were 232 females and 169 males, all aged between two and 12 years next birthday. The fate of 352 children was determined in 1953. Of these, death certificates were sighted for 165. The deaths of 108 were classified as due to cardio-vascular or renal disease—94 as "chronic nephritis", four as "nephritis unspecified", three as "other renal disease", two as "essential malignant hypertension" and four as "nephrosclerosis". Information was available on the state of health of 101 of the living members. Seventeen have hypertension and albuminuria, and three hypertension alone. Thus a total of 127 of the 401 patients are known to have had renal and cardio-vascular disease. An important finding, discussed above, was the length of the period between the admission for plumbism and death from renal disease. The shortest time was five years and the longest 34 years. The period of follow-up was 35 years or more for 91 cases.

Past History of Patients with Chronic Renal Disease.

Further evidence linking chronic renal disease in Queensland with plumbism was obtained from the 67 patients, aged 20 to 49 years, used in the clinico-pathological analysis. Eleven of these, all with nephritis of "undetermined" aetiology, gave a history of plumbism. In one case the exposure had been industrial, and in the remaining 10 the diagnosis was made in childhood. Four of these patients were members of the follow-up series described above.

The Familial Incidence of Chronic Renal Disease.

Eleven members of this series, and siblings of three other members who had high bone lead content, as will be discussed below, gave a history of clinical plumbism. The lead hazard to Queensland children was very widespread. There is now a great deal of evidence that, where a lead hazard for children exists, investigation of children without clinical illness will reveal many instances of marked absorption without much in the way of symptoms (Travers *et alii*, 1956; Bridge 1953; Williams *et alii*, 1933).

Ten members of the group of "undetermined" aetiology, including four with a history of clinical plumbism, had siblings who suffered from chronic renal disease in early adult life. The most logical explanation of the familial incidence of renal disease in Queensland is the excessive absorption of lead by the children of a family when exposed to a common hazard—the house in which they lived.

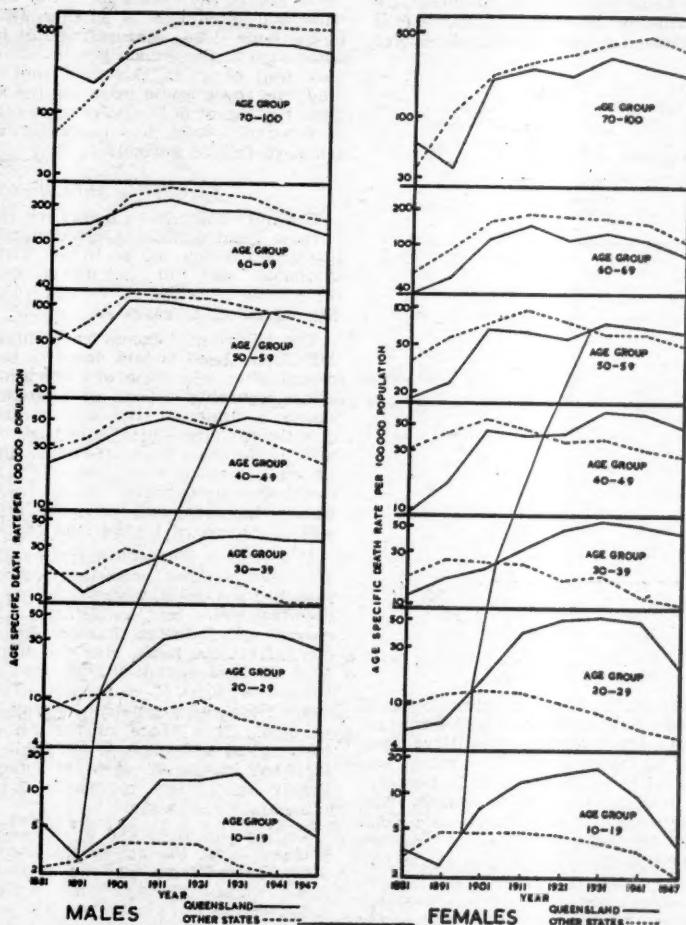
Lead Content of Bone.

General Results.

As in the earlier investigations, a history of previous lead poisoning in 11 cases of chronic renal disease still leaves the majority without a link with plumbism. Fairley (1934) first suggested that this link might be obtained by estimating the lead content of bones, and this has been done in the present study (Henderson and Inglis, 1957).

The lead content of autopsy specimens of skull and rib was estimated for 143 subjects who had suffered from chronic renal disease, including the 67 discussed above, and for 527 without chronic renal disease, who died in Brisbane, Queensland, and also for 179 patients without, and 17 with, chronic renal disease who died in Sydney, New South Wales. The results were recorded in milligrammes of lead per 100 grammes of moist bone. They were divided for analysis in three classes, namely: (a) subjects who were born and died in Queensland; (b) those who were born elsewhere but died in Queensland; (c) those who were born outside Queensland and died in Sydney.

FIGURE I.
Mortality from chronic nephritis. Average annual age and sex specific death rates per 100,000 of population in ten-year groups over ten-year periods from 1876 to 1949, in Queensland and the other States of Australia; 1947 rate is average of four years only. Semi-logarithmic grid. Reprinted by permission from *Australasian Ann. Med.* (1955), 4: 166.



renal disease, who died in Brisbane, Queensland, and also for 179 patients without, and 17 with, chronic renal disease who died in Sydney, New South Wales. The results were recorded in milligrammes of lead per 100 grammes of moist bone. They were divided for analysis in three classes, namely: (a) subjects who were born and died in Queensland; (b) those who were born elsewhere but died in Queensland; (c) those who were born outside Queensland and died in Sydney.

The mean values, in ten-year age groups, for subjects without renal disease are shown in the pairs of lines without circles or crosses in Figure II. It will be noted

that the mean lead content is of the same order in all three classes, and that it is generally somewhat lower in rib than in skull, and in females than in males. It is evident that bone lead levels are essentially similar in the general population of the two States.

The values in cases of chronic renal disease are plotted in Figure II as means in ten-year age groups in class (a), and as individual values in (b) and (c). In subjects who were born and died in Queensland—class (a)—the mean lead content of rib and skull is almost twice as high in the 20 to 49 years age group in both sexes, as in subjects without the disease. In the 50 to 59 years group, the mean for females approaches the normal, while that for males is still high. Over 60 years, the means for both males and females are close to normal.

TABLE II.
Plumbism: Number of Admissions Each Year (1915 to 1935) to the Hospital for Sick Children.

Year.	Number of Admissions.
1915	8
1916	27
1917	32
1918	24
1919	36
1920	27
1921	23
1922	28
1923	40
1924	45
1925	9
1926	35
1927	12
1928	9
1929	12
1930	14
1931	6
1932	6
1933	4
1934	2
1935	2
Total	401

The 20 to 49 Years Age Group.

There were 67 patients suffering from chronic renal disease in the 20 to 49 years age group who were born and who died in Queensland. (All figures refer to milligrammes of lead per 100 grammes of moist bone.) The mean lead content of the skull was 7.31 in males and 7.97 in females; values for rib were 3.48 in males and 4.14 in females. The means for subjects of the same age without chronic renal disease were: skull, 3.91 in males and 3.34 in females, rib, 1.48 in males and 1.26 in females. It was shown, by comparison of logarithms, that the differences between these two classes were significant at the 0.1% level for skull in males and females and rib in females, and at the 1% level for rib in males (Henderson and Inglis, 1957). It was also shown in the same paper that the high lead content in renal disease was not due to retention of normally ingested lead by failing kidneys, but to excessive exposure.

The aetiological diagnosis in the patients with renal disease throws further light on the significance of the high mean bone lead content. The mean lead content in the 13 cases due to generally accepted causes was 3.52 for skull and 1.70 for rib. This amount is of the same order as that for individuals without chronic renal disease. The mean lead content in the 47 cases of "undetermined" aetiology was as follows: skull, 8.45 in males and 8.66 in females; rib, 4.09 in males and 4.53 in females.

Thus, it is clear that the high bone lead content in chronic renal disease in Queensland is associated, not with cases of generally accepted aetiology, such as chronic glomerulonephritis or pyelonephritis, but with the large group of cases, making up the excess mortality, for which no such cause could be found.

The Changes with Age.

Plumbism in childhood as the aetiological agent would also provide a rational explanation of the variation in mean bone lead content in chronic renal disease in the different age groups shown in Figure II. A. The greatest proportion of deaths from this cause would occur in the 30 to 49 years age group, hence the high mean bone lead content. Owing to the decline in mortality already discussed, the number of patients in the 20 to 29 years age group suffering from plumbism would be smaller, with consequent lower mean bone lead content. In the 50 to 59 years group, the excess mortality considered to be due to childhood plumbism is smaller (Figure I), so that the mean bone lead content would be lower, as is well illustrated in the female graphs. In males, however, deaths may well occur at this age from industrial exposure to lead, and these would maintain the average at a high level. Over the age of 60 years, chronic renal disease due to lead is relatively much less common, and the mean in males tends to fall to normal.

Correlation with Mortality Data.

The next point is to determine the actual proportion of chronic renal disease in Queensland in the 20 to 49 years age group which can be linked with plumbism. Mortality statistics do not recognize the clinico-pathological differences described above, and we must therefore consider the sample of 67 cases as a whole.

The criterion of excess lead content of bone also requires definition. Lead is laid down in bone at, and for a short period after, the time of absorption. The metabolic processes occurring in bone after excessive exposure has ended can only diminish, not add to, its lead content. Consequently, the best indicator of past excessive lead absorption will be the bone which (a) has the proportionally higher residual lead content, and (b) is less susceptible to metabolic vicissitudes. Skull fulfills these requirements better than rib, and excessive absorption in this series will be estimated by the lead content of skull.

If the mean lead content of skull in subjects aged 20 to 49 years without chronic renal disease, *plus* twice its standard deviation, is taken as the upper limit of normal, then 14 males and 20 females of the 67 patients with chronic renal disease have an excessively high bone lead content. If the mean *plus* one standard deviation is used, then 23 males and 23 females have a high bone lead content—a total of 46 persons. Thus, in at least half the sample the chronic nephritis may be considered to be due to lead. That those of the 34, or 46 cases for which histological sections were available are, with one exception, included in the 47 cases of "undetermined aetiology" is highly significant in itself, but not relevant to the immediate discussion.

During the three and a half years in which the sample was collected, the age-specific death rate in the 20 to 49 years group from chronic nephritis, hypertension with heart disease, hypertension without heart disease and infections of the kidney was 115 per 100,000 in Queensland and 52.4 in the other States of Australia, the rates being calculated on 1947 population to avoid the effect of migration. Thus, approximately half of the deaths in Queensland represent excess mortality. If lead is the sole cause of at least half the deaths in the sample. This has been done, and it is concluded that lead alone can account for the whole of the excess mortality from "chronic nephritis" in Queensland. It also follows that, in children at least, chronic renal disease can result from excessive lead absorption of a degree insufficient to produce clinical illness at the time when it occurred.

Summary.

No direct evidence that childhood plumbism was responsible for the high incidence of chronic renal disease in Queensland can be obtained today. However, the several lines of circumstantial evidence reviewed in this section are independent and consistent. There was a high incidence of renal disease in persons known to have had lead poisoning in childhood; a frequent history of childhood

plumbism was obtained in the chronic renal disease group investigated; a significantly raised bone lead content was found in that group; there was a correlation in familial incidence; bone lead values correlated with the age incidence of chronic renal disease, and with the historical sequence in childhood plumbism; and there was a correlation between the frequency of high bone lead values and the excess mortality from chronic renal disease in this State. Of greatest significance is the finding that a history of childhood plumbism and excess bone lead values occurred only in a particular group of cases which had been separated on independent clinico-pathological grounds.

This combination of findings, it is held, leaves no room for doubt that the excess mortality from chronic renal

itself is known to produce the same type of lesion as that in Queensland cases of "chronic nephritis", and when there is evidence tending to exclude them, the possibility that the other constituents of paint may play a part in the production of the lesion are remote.

Chronic Glomerulonephritis.

Cilento (1932) suggested, on quite inadequate grounds, that subclinical scarlet fever might be the cause of Queensland's "chronic nephritis". His arguments are effectively disposed of by Nye (1933). However, Croll (1929) gave figures showing that the mortality from "acute nephritis" in Queensland was higher than that in the other States during the years 1907 to 1926. He pointed out that this excess mortality occurred in the same age groups as that

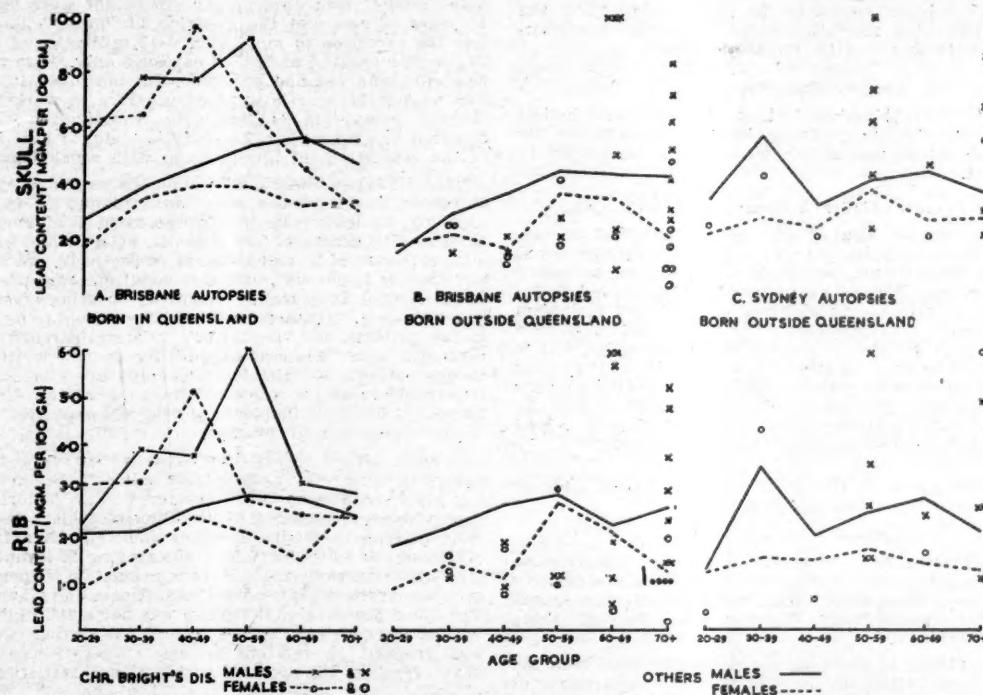


FIGURE II.

Bone lead content of rib and skull in subjects aged over 20 years. A, born in Queensland, died in Queensland at Brisbane; B, born outside Queensland, died in Queensland at Brisbane; C, born outside Queensland, died in New South Wales at Sydney. Mean values in ten-year age groups are plotted throughout for subjects without chronic Bright's disease, designated "others". Values in cases of chronic Bright's disease are plotted as means in ten-year age groups for subjects in A, and individually for subjects in B and C. Reprinted by permission from *Australasian Ann. Med.* (1957), 6:145.

disease in Queensland has been due solely to lead absorption in childhood.

OTHER POSSIBLE CAUSES OF THE CHRONIC NEPHRITIS OF QUEENSLAND.

Other Constituents of Paint.

According to manufacturers, the other constituents of the lead paint used in Queensland before 1920 were linseed oil and a very small proportion of "driers", which were metallic salts having a catalytic action. In the course of drying, polymerization of the linseed oil occurs, with the production of resins which are very insoluble and inert substances. The same substances were used in the zinc paint which replaced lead on surfaces accessible to children, with subsequent decline in plumbism and mortality from chronic nephritis. Hypothetically, zinc could have had a "protective" effect. However, it will be shown later that lead has caused chronic renal disease outside Queensland in workers not associated with paint. Thus, when lead

from "chronic nephritis", and, on these grounds, concluded that misdiagnosis of chronic nephritis as acute nephritis was responsible.

The present investigation provides the following arguments against glomerulonephritis as the cause of Queensland's excess mortality from chronic nephritis. (i) The clinical and histological evidence is against glomerulonephritis. (ii) Acute glomerulonephritis in the age groups shown by Croll would not explain the features of chronic nephritis mortality described above. (iii) Physicians in practice at the time state that there was no exceptional incidence of acute nephritis among children and adults. (iv) The records were obtained of all patients classified as having "acute nephritis" at the Brisbane General Hospital and the Metropolitan Hospital for Infectious Diseases, Brisbane, during the years 1930 and 1931. These were years in which the mortality in Queensland was higher than in other States. There were 28 patients, six of whom died, one from acute nephritis with pulmonary

oedema, and one from toxic effects of "Novarsenobillon". Four patients had been given the diagnostic label "subacute nephritis", which is classified under "acute nephritis" as a cause of death. Of these four, three gave a history of "kidney trouble" for 23, five and two years respectively. Autopsy had been performed on the last of these, and the kidneys were found to be small and contracted. These patients were obviously incorrectly classified. Of the 22 patients who did not die, only 11 appear to have been suffering from true acute glomerulonephritis, four of them as a result of scarlet fever. Two of these latter patients had albuminuria as the only manifestation. As the Brisbane General Hospital was the only large public hospital in Brisbane at the time, and the Metropolitan Hospital for Infectious Diseases the only infectious diseases hospital, it can be safely concluded that there was no high incidence of acute glomerulonephritis in the community, and no exceptionally high mortality in those contracting the disease. The high mortality recorded in the Registrar-General's data was due to diagnostic errors.

Chronic Pyelonephritis.

There is no epidemiological, clinical or pathological evidence that chronic pyelonephritis was responsible for any of the excess mortality from "chronic nephritis" in Queensland.

Other Factors Acting in Conjunction with Lead.

There is no evidence of any factor operating in conjunction with lead in the production of chronic renal disease in Queensland, and it does not appear necessary to postulate one. The follow-up investigation showed that a quarter to a third of the children with clinical plumbism died of chronic renal disease in the next 40 years. Such a proportion, on general principles, is not excessive, but it may possibly be due to a greater susceptibility of the young kidney. There are no comparable figures for adults or for children outside Queensland, but the question may be decided when the relationship of contracted kidneys to lead is finally investigated in other parts of the world.

LEAD POISONING AS A CAUSE OF CHRONIC RENAL DISEASE OUTSIDE AUSTRALIA.

Summary of Literature.

Lead poisoning as a cause of chronic renal disease has been discussed in the literature for about a century. In recent years, some doubt has been cast on the causal relationship, particularly in America (Mayers, 1947; Johnston, 1948).

Olivier (1863) is generally considered to have been the first to draw attention to the frequent occurrence of albuminuria in plumbism. He gives a clinical description of 15 examples of albuminuria in workers suffering from plumbism. Autopsy findings in one patient, a man, aged 36 years, included granular contracted kidneys. In 1881, Dickinson reported that, of 42 workers in lead trades who died of disease or accident, 26 had granular kidneys.

Oliver (1891) described chronic renal disease as a sequel of plumbism, and reiterated it in 1908 in the following words: "... in chronic plumbism ... the kidneys are small and contracted, the capsule is firmly adherent, and on microscopic examination there are evidences of interstitial nephritis."

Legge and Goadby (1912) give comparative mortality figures from specific causes among males engaged in certain occupations during the years 1900 to 1902. The mortality from Bright's disease was as follows: all males, 35; lead workers, 160; file makers (lead hazard), 134; painters and plumbers, 74. Their findings in a fatal, typical case of chronic plumbism in a man, aged 44 years, included contracted granular kidneys, with "interstitial fibrosis" on microscopic examination. They imply that this was an accepted complication, but suggest that alcohol may be an aggravating factor.

Machwitz and Rosenberg (1916) found that three of 95 patients with "benign nephrosclerosis" and nine of 35 patients with "malignant nephrosclerosis" had been lead workers.

Russell (1929) described, among cases which she classified as "nephritis repens", one patient with "possible exposure to lead", and one who was a lead worker for 21 years. Both had small contracted kidneys.

Mayers (1929) examined 381 lead workers in the factory. The group contained no cases of incapacity due to acute lead poisoning. Of the workers, 89% were less than 50 years of age. The incidence of arteriosclerosis was estimated, no criteria being given, and the final conclusion on the relationship between lead and arteriosclerosis was: "The present study does not demonstrate this relationship very convincingly." On the relationship of lead and hypertension, the conclusion was: "The series appears to indicate that a relationship does exist." No specific attempt to determine the presence of renal disease was made.

Belknap (1936) took the blood pressure of 81 workers with "heavy" lead absorption. Sixty-eight were less than 40 years of age, and the criterion of "heavy" absorption was the excretion of more than 0.15 milligram of lead in 24 hours, measured at "peak" exposure only. Five patients had colic, and one had paralysis. He concluded that there was no significant rise in blood pressure in workers with "heavy" absorption of lead. No investigation of renal function was made, but the study is included here because of the association of hypertension with renal disease.

Gant (1938) published, *inter alia*, the results of coroners' autopsies on 21 persons who had a history of industrial exposure to lead resulting in increased lead content of tissues. The deaths of two patients, aged 56 and 31 years, with exposure of 21 and 10 years respectively, are ascribed to "chronic nephritis", and this condition was present in another, aged 36 years, in whom the duration of exposure was unknown. "Glomerulonephritis" was said to be present in two patients, and "nephritis", "bilateral parenchymatous nephritis" and "bilateral suppurative pyelonephritis" each in one patient. No histological details are given, so it is impossible to assess the exact meaning of the diagnostic terms. At least the incidence of "chronic nephritis" is high in the group at younger ages.

Dreesen (1941) reported an extensive survey of the lead hazard in the electric accumulator industry. Seven hundred and sixty-six workers were examined. The factories were supervised, and no cases of disabling plumbism were seen. Nine patients were diagnosed as suffering from incipient plumbism, and 168 from lead absorption. Relevant to the present discussion, are his conclusions on hypertension, arteriosclerotic-hypertensive heart disease and albuminuria. The blood pressure of the group was not much higher than that of workers not exposed to lead. A similar conclusion was reached in relation to arteriosclerotic-hypertensive heart disease, although an increase, not statistically significant, was noted in the "lead-affected" members. Albuminuria was found twice as frequently among "lead-affected" workers, a proportion regarded as statistically significant. Apart from microscopic examination of urine, which showed no particular abnormality, no other assessment of renal function was made.

Chapman (1941) lists the results of 10 autopsies at the Massachusetts General Hospital between 1912 and 1927, on subjects who were either painters dead of Bright's disease, or patients with lead poisoning at the time of death. One patient appears to have suffered from chronic glomerulonephritis and one from chronic pyelonephritis. Six had "vascular nephritis" of varying degree. The most severe degrees were in patients aged 44, 45 and 43 years with combined kidney weights of 204, 138 and 135 grammes respectively.

Lane (1949) makes an excellent review of the incidence of plumbism in Great Britain. His graphs illustrate the fall in the number of cases since 1900. He draws attention to the lag of some 25 years between the fall in the number of cases and the fall in deaths, suggesting that deaths from chronic renal disease could be responsible. He states that, in the 15 years prior to writing, he had seen nine deaths from hypertension with renal failure occurring in a group of 150 workers exposed in the "bad days" of the industry to more than five milligrammes of lead per 10 cubic metres of air. The clinical picture was the same in all cases. The average age at death was 48.4 years. A brief description of

the histological picture is given. Lane dismissed this finding as of little statistical significance. However, the death rate in males aged 45 to 54 years from "arteriosclerotic kidney" and "other chronic and unspecified nephritis" in England and Wales in 1940 was 334.6 per million, and nine in 154 is equivalent to 60,000 per million. He also compared the blood pressure of 56 workers exposed over a period of 20 years, initially to 2.5 milligrammes and later to 1.5 milligrammes per 10 cubic metres of air, with that of controls. There was no significant difference between the groups. Three of the lead workers and two controls had albuminuria. No other tests of renal function were made.

Greenfield and Gray (1950) reported studies of a selected group of 40 patients, who had "either acute lead poisoning or developed an acute toxic episode after many years of lead absorption". The heart was normal in all patients except one with rheumatic heart disease; three had "transient hypertension"; the urine was normal in all. The original description of the cases from which the selection was made (Gray and Greenfield, 1937), shows that there were 54 cases of acute poisoning in men exposed for periods ranging from two weeks to three months, and 38 cases of chronic absorption with acute toxic episode. The description of clinical and laboratory findings makes it clear that the plumbism was mild. Of the 38 patients with chronic absorption, elevation of blood pressure was noted in eight, cardiac hypertrophy in 10, and one patient, exposed for 25 years, died with contracted kidneys. It is obvious that the group of 40 patients was so highly selected that general conclusions on the effect of lead on the cardio-vascular and renal system based on it are not justified.

DISCUSSION.

The positive evidence in favour of lead causing a chronic renal lesion is as follows: (i) the presence at autopsy of a chronic renal lesion in lead workers, and a history of lead exposure in many patients with chronic renal disease; (ii) mortality data for lead workers in Great Britain; (iii) the clinical experience of industrial hygienists prior to the introduction of effective preventive measures.

However, it has become more difficult to demonstrate chronic renal disease among active lead workers, as illustrated by the surveys of Mayers (1929), Belknap (1936) and Dreesen (1941), and doubt has been expressed that lead produces a chronic renal lesion (Mayers, 1947; Johnstone, 1948).

The last 60 years have seen a tremendous change in the conditions of lead workers. Legislation introduced after representations by the industrial hygienists at the end of the last century, increased knowledge of the nature of the poisoning and closer medical supervision, have resulted in a great reduction in the hazard of occupational lead exposure. Not only was actual exposure reduced, but the closer medical supervision detected intoxication at a much earlier stage, and steps were taken to prevent a recurrence in the individuals concerned. The publication by Lane (1949) shows clearly the decrease in the frequency of plumbism in Great Britain. However, his graphs give no indication of the even greater decrease in severity of the disease. The same general picture appears to have developed in all the major industrial nations.

The findings in investigations such as those of Mayers (1929), Belknap (1936) and Dreesen (1941), and that of Lane (1949) relating to hypertension, have to be considered against this background.

The following general facts apply of these investigations: (i) They were performed in carefully supervised factories, where exposure was reduced to a minimum, and intoxication detected early. There was no severe plumbism, and it can be taken that the dose of lead was small. (ii) The workers examined were all actively engaged in the lead industry. This necessarily implies a large element of selection; it would exclude workers who have left the industry because of plumbism itself, or because of other illnesses which may have been manifestations of hypertension, arteriosclerosis or renal disease. It could even be argued that those remaining in the industry were those

with either the least absorption of lead or the greatest natural resistance to its effects. The age distribution of the workers examined in these surveys shows that they are predominantly in the younger groups, suggesting a considerable turnover, with many leaving the industry before they reach the older groups. Estimates of the long-term effects of lead by this type of investigation will never be reliable until workers who have left the industry are included, and even then a worker who leaves after one attack of acute intoxication may have had a relatively small dose of lead.

Apart from the above-mentioned general considerations in relation to these investigations, some examination of the data as possible criteria of renal disease is required. The presence of hypertension and of albuminuria, and in some cases the findings on microscopic examination of urine, are recorded. It will be shown in a future paper that quite severe renal damage due to lead can exist in the presence of very mild hypertension, with intermittent slight albuminuria and normal microscopic findings in urine. Mild cases could easily be missed in these surveys.

Thus it appears that the papers of Mayers, Belknap and Dreesen, and that part of Lane's paper dealing with hypertension, cannot be used as evidence against the general thesis that lead produces a chronic renal lesion in humans.

The most reliable way of obtaining further information on the subject would be by careful clinico-pathological analysis of autopsy cases of chronic renal disease, in conjunction with the estimation of the lead content of bone as previously described (Henderson and Inglis, 1957).

There is considerable uncertainty as to how lead produces the chronic renal lesion. Hypertension, arteriosclerosis and granular contracted kidneys have been the usual findings, but it has not yet been decided which is primary. The opinion of Legge and Goadby (1912) that arteriosclerosis was primary has had a large influence on thought on the matter, but has never been definitely confirmed. In a future paper, evidence will be presented to show that lead can affect the kidney tissue primarily, hypertension and arteriosclerosis occurring subsequently.

SUMMARY.

There is a great deal of evidence that lead can produce a chronic renal lesion in man. Critical analysis of a number of surveys of lead workers, in which a high incidence of hypertension, arteriosclerosis or renal disease was not found, shows that they cannot be used as evidence against this general statement.

CONCLUSION.

The story of lead poisoning in Queensland children is a most interesting one, which reflects the greatest credit on two former practitioners—Alfred Jefferis Turner and John Lockhart Gibson. These two men first recognized the disease in the community. They traced the source of the poison, and initiated a campaign for its removal, which culminated in legislation in 1922 restricting the use of lead paint. As a result, plumbism in Queensland children diminished greatly during the next decade. History contains few better examples of the practice of medicine in its widest sense. Recent legislation forbidding the use of lead pigments in paint consolidates their achievements.

Gibson and Turner confined their investigation to actual plumbism, but, in common with other practitioners of their day, they believed, on clinical grounds, that the high incidence of chronic renal disease in Queensland was due to lead poisoning in childhood. The present investigation, combined with those which preceded it, establishes that belief with greater certainty.

The results reported in this paper have more than local application. Plumbism, both industrial and non-industrial, both clinical and sub-clinical, occurs in many parts of the world, yet lead is not usually considered when the aetiology of chronic renal disease is investigated. It is clear that the aetiology of contracted kidneys might well be reviewed outside Queensland in the light of this paper, and the estimation of the lead content of bone is the tool which would make that review effective.

If lead nephrosclerosis does occur to any degree outside Queensland, it has most probably been diagnosed in the past as hypertensive nephrosclerosis or as chronic pyelonephritis. A smaller proportion of cases may have been called chronic glomerulonephritis, and others gout.

The paper also poses a problem to the lead-using industry of determining eligibility for compensation.

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REFERENCES.

BELKNAP, E. L. (1936), "Clinical Studies on Lead Absorption in the Human. III. Blood Pressure Observations", *J. Indust. Hyg. & Toxicol.*, 18: 380.

BRIDGE, A. (1958), "Lead Intoxication in Three Families", *M. J. AUSTRALIA*, 2: 62.

CHAPMAN, E. M. (1941), "Observations on the Effect of Paint on the Kidneys with Particular Reference to the Role of Turpentine", *J. Indust. Hyg. & Toxicol.*, 23: 277.

CILENTO, R. W. (1932), "Commonwealth of Australia: Interim Report of an Official Inquiry into the Chronic Nephritis of Queensland with Special Reference to Plumbism in Children".

Council of Queensland Branch of British Medical Association (1923), "An Historical Account of the Occurrence and Causation of Lead Poisoning among Queensland Children", *M. J. AUSTRALIA*, 1: 148, 282.

CROLL, D. G. (1929), "The Incidence of Chronic Nephritis amongst Young People in Queensland", *M. J. AUSTRALIA*, 2: 144.

DICKINSON (1881), "Treatise on Albuminuria", New York, 110; cited by Fishberg, A. M. (1954), "Hypertension and Nephritis", Philadelphia, 743.

DREBSEN, W. C. (1941), "The Control of the Lead Hazard in the Storage Battery Industry", United States Public Health Service Bulletin, No. 262.

FAIRLEY, K. D. (1934), "A Review of the Evidence Relating to Lead as an Aetiological Agent in Chronic Nephritis in Queensland", *M. J. AUSTRALIA*, 1: 600.

GANT, V. A. (1938), "Lead Poisoning: 51 Fatal Cases of Suspected Lead Poisoning and 46 of Non-fatal Lead Poisoning", *Indust. Med.*, 7: 679.

GISSON, J. L. (1904), "A Plea for Painted Railings and Painted Walls of Rooms as the Source of Lead Poisoning amongst Queensland Children", *Australasian M. Gaz.*, 23: 149.

GRAY, I., and GREENFIELD, I. (1937), "Lead Poisoning in the Community", *New York State J. Med.*, 37: 1971.

GREENFIELD, I., and GRAY, I. (1950), "The Failure of Lead Poisoning to Affect the Heart and Blood Vessels", *Am. Heart J.*, 39: 430.

HALFORD, A. C. F. (1897), Medical Society of Queensland (Report of Meeting), *Australasian M. Gaz.*, 16: 519.

HENDERSON, D. A. (1954), "A Follow-up of Cases of Plumbism in Children", *Australasian Ann. Med.*, 3: 219.

HENDERSON, D. A. (1955), "Chronic Nephritis in Queensland", *Australasian Ann. Med.*, 4: 163.

HENDERSON, D. A., and INGLIS, J. A. (1957), "The Lead Content of Bone in Chronic Bright's Disease", *Australasian Ann. Med.*, 6: 145.

JOHNSTONE, A. B. (1948), "Occupational Medicine and Industrial Hygiene", St. Louis, 234.

LANE, R. E. (1949), "Care of the Lead Worker", *Brit. J. Indust. Med.*, 6: 125.

LEGGE, T. M., and GOADBY, K. W. (1912), "Lead Poisoning and Lead Absorption", London.

MACHWITZ, H., and ROSENBERG, M. (1917), "Zur Klinik der vaskulären Schrumpfniere", *Deutsche med. Wochenschr.*, 1188.

MATHEWSON, T. H. R. (1917), "British Medical Association News" (Report of Meeting), *M. J. AUSTRALIA*, 2: 364.

MAYERS, M. R. (1927), "A Study of the Lead Line, Arteriosclerosis, and Hypertension in 381 Lead Workers", *J. Indust. Hyg. & Toxicol.*, 9: 239.

MAYERS, M. R. (1947), "Industrial Exposure to Lead", *Occup. Med.*, 3: 77.

MURRAY, R. E. (1939), "Plumbism and Chronic Nephritis in Young People in Queensland", Commonwealth of Australia, Department of Health Service Publication (School of Public Health and Tropical Medicine), No. 2.

NYE, L. J. J. (1929), "An Investigation of the Extraordinary Incidence of Chronic Nephritis in Young People in Queensland", *M. J. AUSTRALIA*, 2: 145.

NYE, L. J. J. (1931), "Saturnine Renal Dwarfism", *M. J. AUSTRALIA*, 2: 818.

NYE, L. J. J. (1933), "Chronic Nephritis and Lead Poisoning", Sydney.

OLIVER, T. (1891), "Goulstonian Lectures on Lead Poisoning in its Acute and Chronic Manifestations", *Brit. M. J.*, 1: 685.

OLIVER, T. (1908), "Diseases of Occupation", London.

OLLIVER, A. (1863), "De Falbiminurie saturnine", *Arch. gén. de médecine*, 2: 530.

RUSSELL, D. S. (1929), "A Classification of Bright's Disease", Medical Research Council of the Privy Council, Special Report Series No. 142.

TELEYK, L. (1937), "A Note on Blood Pressure in Lead Poisoning", *J. Indust. Hyg. & Toxicol.*, 19: 1.

TOMPSITT, S. L. (1936), "The Distribution of Lead in Human Bones", *Biochem. J.*, 30: 1851.

TRAVERS, E., RENDLE-SHAW, J., and HARVEY, C. C. (1956), "The Rotherham Lead Poisoning Outbreak", *Lancet*, 2: 113.

TURNER, A. J., GIBSON, J. L., LOVE, W., HARDIE, D., and BANCROFT, P. (1892), "Notes on Lead Poisoning as Observed Among Children in Brisbane", *Transactions of the Intercolonial Medical Congress of Australia*, Third Session, September, 76.

VIDORTCHIK, N. A. (1935), "Lead Intoxication in the Aetiology of Hypertension", *J. Indust. Hyg. & Toxicol.*, 17: 1.

WILLIAMS, H., SCHULZE, W. H., ROTHSCHILD, H. B., BROWN, A. S., and SMITH, F. R. (1938), "Lead Poisoning from Burning Battery Casings", *J. A. M. A.*, 100: 1485.

SOME ASPECTS OF THE MANAGEMENT OF DIABETES.

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THE subject of tonight's talk, the management of diabetes, is one which has received a great deal of attention for many years, and which will continue to be an even more pressing problem as our population of diabetics increases. In a talk such as this, it is possible to cover only small facets of the subject.

The disease has been recognized since Egyptian times, but it was not until the isolation of insulin by Banting and Best in 1921 that a new era dawned for diabetics. Suffice it to say that the life expectancy of a child aged 10 years who developed diabetes has risen from two years to 50 years.

However, although the use of insulin has led to a gratifying prolongation of life, it has not turned out to be the panacea. Certainly the fear of diabetic ketosis as a cause of death has been almost entirely eliminated; staphylococcal infections have become much less prevalent; tuberculosis and urinary tract infections are less frequently encountered. But, on the debit side, an increasingly important part is being played by the degenerative complications of the disease, particularly cardio-vascular-renal disorders, such as retinal lesions and serious lesions that result from diabetic neuropathy.

At this stage one must ask what we mean by "diabetes". Does a definition such as that given by Cecil, that diabetes is "a disorder of carbohydrate metabolism characterised by hyperglycæmia and glycosuria", cover the whole picture? If that was so, then the disorder could easily be eliminated by the use of insulin. Insulin therapy has allowed a greatly lengthened time of study of patients with diabetes, which has revealed a more interesting pattern of associated disabilities. This pattern appears most prominently in the relation between pregnancy and diabetes, with the high incidence of babies weighing over 10 pounds at birth. This tendency to produce large babies occurs not only in those mothers under treatment for diabetes, but also in those in whom clinical diabetes does not develop for many years after this birth. The incidence is greatest in the five years prior to the onset of clinical diabetes, but it is significant for as long as 20 years before the onset of overt diabetes. The presence of a genetic factor is suggested by the similar incidence of large babies whose fathers are both in the overt diabetic state and in the years before diabetes becomes obvious (Jackson, 1955). Diabetic fathers beget 14% of the overweight babies, while among the diabetic and pre-diabetic mothers the proportion of overweight babies is nearly 30%, suggesting an additional maternal

¹ Read at a meeting of the South Australian Branch of the British Medical Association on August 29, 1957.

environmental factor. These diabetic parents are also responsible for a very high proportion of children who show clinical diabetes and other interesting characteristics. White (1953) has shown that, on the average, the children of diabetic parents are heavier and taller than a corresponding group of children from normal parents. In addition, the incidence of diabetes in these children is much higher. In the general population one child in 2500 developed diabetes, whilst of the children of diabetic and pre-diabetic mothers 23% showed diabetes; in 9% it was clinical and in 14% it was borderline, shown only by an abnormal response to the glucose tolerance test. Among the offspring of diabetic fathers the percentages were 21 and nine respectively, whilst when both parents were diabetic the percentage was 62. In addition to the 17% incidence of congenital defects in White's series, Ditzl (1954) has shown an apparently well-defined abnormality of the vascular pattern of the smaller vessels in the conjunctiva when they are examined at microscopic level. This abnormality occurred in 75% of the children classified as diabetic or as "borderline" diabetic. A positive correlation was found between the degree of vascular change in the smaller blood vessels of the conjunctiva, the abnormal glucose tolerance test and the high growth rating. This vascular abnormality may be related to the high incidence of occlusive lesions in the digital arteries and smaller vessels of the feet, where such lesions are often far in advance of the generalized arteriosclerotic changes. There is also the very grave incidence of coronary artery disease, the total rate of which is four to five times greater than in the normal population, and of which the incidence in women equals that in men. These observations suggest some basic vascular abnormality, the nature of which is uncertain. The additional finding of a variety of abnormalities in the fetus of the diabetic mother supports the view that the underlying defect is far more fundamental than a simple upset of glucose metabolism from a lack of insulin and the disorder could be considered as an inborn error of metabolism.

It is against this background that our concepts of treatment are seen. One view is that these various abnormalities, particularly the vascular lesions, are independent of the hyperglycæmia, etc., and are not affected by efficient treatment with insulin. If this was so, then therapy in many cases would be pointless. However, Root and Joslin show that there is a greatly lessened incidence of complications in these patients who undergo strict therapy; and there is evidence that hyperglycæmia *per se* can produce some of these degenerative vascular lesions in an otherwise normal animal. Thus, one of the fundamental tenets of any therapy is that treatment should be used with the utmost energy to maintain the blood sugar levels within the physiological range—that is, between the values of 80 and 160 milligrammes per 100 millilitres. I will be the first to admit that this ideal is more often sought after than obtained; but unless such an ideal is held, treatment with a potent drug is pointless.

Our weapons to achieve this result are diet and insulin. Our patient has a much heavier armament to use against us, and this must always be remembered. With the patient's cooperation we can manipulate diet and insulin dosage; but we cannot alter the effect of emotional upsets, of environmental worries, of lack of sleep or of weather changes, whilst we can in part allay the changes brought about by trauma, infection, exercise, pregnancy, etc. One must stress again and again that it is only by the patient's complete cooperation in dietary measures and insulin dosage that we can achieve a useful result, and that even at best we have only two factors (that can be varied voluntarily) with which to oppose some seven or eight unknown factors. This at once brings me to the point that a diet restricted and controlled to an obsessive degree is not only an excessive burden on the patient, but is also unlikely to be carried out. Root and Joslin state, as one of their criteria for adequate control of diabetes mellitus, the necessity for all diets to be weighed for at least 80% of the time. Undoubtedly these rigid controls have value, but they must make it almost impossible for the patient to live with his disease and with his fellow men without developing a rather severe

obsessional state. The violent swing away from this to the completely "free diet" was followed by over-eating, overweight and a rising blood sugar level necessitating an increasing dose of insulin—all in rather a vicious circle, with increased incidence of complications as an end result. The present widely held view is that regularity of food intake, particularly carbohydrate, must be one of the governing factors in any diabetic diet. The fact that the diabetic cannot produce insulin on demand must be taken into account, and the intake of carbohydrate fixed within relatively inelastic limits and spaced according to the type of insulin used. Carbohydrate is needed not only to make any diet palatable, but also to supply Calories. Apart from this, the diet must be sufficient to maintain the patient's weight at a few pounds below the average weight for his height and age, and enable him to do a full day's work whether in the office or in stacking timber. On no account must we allow a diabetic to become fat, as this radically increases the insulin requirement. The carbohydrate ration will usually supply about two-fifths of the total Calories; protein should be given in optimum amounts with fat to bring up the Calorie intake to the required level. An exception to this rule is the fat patient with glycosuria, for whom rigorous Calorie restriction is essential, who is put on a diet of 1300 Calories or less, restricted to 100 grammes of carbohydrate daily. On such a reduced diet, the conscientious patient will lose two to three pounds a week with certainty. We all know the stories and excuses that accompany failure to lose weight; some are plausible, and some fascinating. Recently a butcher weighing 16 stone, who failed to lose weight on a 1200 Calorie diet, assured me that, as so much fat from the atmosphere of his shop entered his body through the pores of his skin, his diet was not of the least value. One only has to recall the signal success that can be obtained by a cooperative patient to realize the answer to such failures; but we must remember that an interference with the patient's appetite-regulating centre may occur in diabetes, and this will sometimes cause great difficulty in cooperating on any dietary regime. In our diabetic clinic we use a system of moderately rigid control of total carbohydrate intake, with a wide variety of transfers, all measured by a domestic scale.

For whom is a dietary régime alone allowable? Firstly, it is allowable for those obese patients with glycosuria and hyperglycæmia in whom no ketosis is present, and in whom weight reduction is imperative. Frequently weight reduction is followed by a return of blood sugar level to the normal range, where it remains until such time as infection, trauma etc. throw the control out of balance.

John (1950) recorded the histories of 25 patients followed for up to 20 years, in whom diet alone was required to control their hyperglycæmia. On occasions these patients required insulin to overcome specific emergencies, such as acute infections, but in the main, carried on for this long period on diet alone. Unfortunately, he makes no reference to the incidence of complications in the cardio-vascular-renal field.

Then comes the borderline group of persons, in whom diet will keep the blood sugar level in a range of, say, 150 to 220 milligrammes per 100 millilitres. What is to be done here? As we stated at a meeting of the Diabetic Association several months ago, the extreme view is that any patient with an elevated blood sugar level should be given insulin whether or not there are any complications. This radical view has many eminent protagonists. At our diabetic clinic, in the absence of any evident complication, such a patient is checked at regular intervals for retinal, renal, neurological and cardio-vascular changes. If none of these changes appear in advance of his age, then treatment with diet alone can continue. Whether one is dooming such a patient to blindness, uremia or gangrene is not absolutely certain; but in the older age group one has to be reasonable, and after the age of 65 years there are often good reasons for delaying insulin therapy.

Diet must be supplemented with insulin in the treatment of all patients with a juvenile type of diabetes, with symptoms of thirst, polyuria and weight loss, glycosuria and ketonuria. It must be supplemented in the treatment of those patients in whom diet alone does not reduce the

blood sugar level when a satisfactory weight has been reached, and in those in whom dietary restriction only leads to general lassitude, malaise, etc.

What is going to be our best method of approach, and what type of insulin shall be used? At the moment we have seven types of insulin readily available, the majority in two strengths and a few in three or four strengths, allowing a total of 15 or more potentially different injections. The trend towards the use of modified insulin has been proceeding gradually with protamine zinc insulin as the first major advance. With protamine zinc and protamine zinc soluble mixtures, either made by the patient or in the form of "N.P.H.", a ready range of insulins active over the 24 hours was available. Why, then, were the "I.Z.S." insulins introduced? American authors could find no good reason for this at first, and claimed that they were an unwanted addition. It is a major advance that they are less contaminated and less liable to produce the common, irritating sensitivity reaction, but even in this respect they are not as good as earlier reports anticipated. Insulin semi-lente, with an action lasting for 8 to 12 hours, and ultra-lente, acting for 20 to 30 hours, are the basic components, and Höllas Möller's 3 to 7 mixture, lente, is the most popular combination, giving, in a majority of instances, satisfactory control. Owing to the fact that "I.Z.S." was coming on the market in the early days of the diabetic clinic at the Royal Adelaide Hospital, we have used this insulin extensively; now we are treating about 280 patients with it, as opposed to 164 patients with other insulins. Lente insulin is used for practically all new patients. Those patients who are being treated with other insulins and in whom control is poor are usually changed, but unless poor control is evident there is no justification to change the insulin type.

How is the new patient approached? Provided that ketosis is not a problem, his diet is estimated roughly to meet his requirements, ranging from 1500 to 2500 Calories in the first instance. "I.Z.S." lente is given, commencing with doses of 16 to 20 units daily, and the patient is examined daily at the clinic for the first few days. Daily visits are essential, first to enable the patient to be taught about his syringe, his injection techniques, the testing of his urine, etc. As he has to make a daily visit, it is urgent for the patient to master technique rapidly. In very few instances has it taken more than four or five visits to the clinic to educate the patient sufficiently well to make him self-reliant. It is a tribute to Sister L. E. Gray and Sister M. Gall of the hospital clinic that these excellent results are obtained. The education has been satisfactory in patients whose ages range from 13 to 78 years, and most impressive has been the joy with which one patient, aged 78 years—a retired engine driver—announced that he was proficient in giving his own injections. Weekly examinations by the medical officer then follow, with instructions to increase doses of insulin by four units every fourth day if the urine tests still show heavy sugar content. When the urine becomes sugar free, urine and blood sugar levels are checked; fasting 11 a.m. and 2 p.m. levels are used, to ensure that urinary readings are of some value for future control. However, we must beware of trying to treat all patients with a single daily dose. This may be the ideal, but when two injections a day give the best control, then this fact must be appreciated. Like the diet, insulin dosage must be tailor-made to fit the patient. In doses of up to 64 units daily, our experience has been that single injection of either "I.Z.S." lente or protamine zinc soluble insulin has every chance of being perfectly satisfactory, and our dosage scale supports this. Above this dose of 64 units we have serious objections, based on the fact that one cannot be sure of an even range of blood sugar levels on a single large injection. Since the practice of checking three-hourly blood sugar levels through the 24 hours has been instituted, a few very unpleasant surprises have been found, with blood sugar levels between the hours of 9 p.m. and 6 a.m. falling as low as 20 milligrams per 100 millilitres. This, too, raises the serious practical problem of dealing with the hypoglycemia that may be associated with the use of modified insulins. The patient, having become habituated to this degree of hypoglycemia, may suffer only from symptoms of headache, tiredness, amnesia or slight

confusion. But when he has passed that point and become unconscious, we are immediately at a stage when blood sugar levels are so low that potentially lethal cerebral damage will occur within half an hour or so, and thus we are exposing our patient to an undue risk. The acute onset of hypoglycemia due to the injection of soluble insulin, and the dramatic recovery when relief is obtained, are well known; but far more worrying is the rather helpless struggle one has with a severe reaction from the use of a modified insulin, when the blood sugar level can be raised to levels well above 300 milligrams per 100 millilitres, yet the patient may never regain consciousness and will ultimately die. Fortunately, this is rare; but not so rare are the amnesia and slight, but distinct, personality change that may follow such an incident of a briefer nature. This may have its advantages. Prior to such a prolonged reaction, one non-cooperative patient was a difficult, quarrelsome husband. After 24 hours in a state of semi-coma, he was a very changed and docile person, almost as though he had undergone a leucotomy; his wife was overjoyed with the result of the excellent treatment, but she was unaware of the gravity of the situation.

Although we have one or two patients who are adequately controlled on 120 to 140 units of lente insulin per day, I feel strongly that only in exceptional circumstances should more than approximately 60 units of a modified insulin be administered in a single dose. For a complete approach to insulin dosage one is referred to an excellent review by Heale (1957).

For the patient on insulin, constant reiteration of the signs and symptoms of hypoglycemia is essential, until one finds that the patient begins to teach his doctor new and individual symptoms. For the same type of insulin the individual patient has a stereotyped pattern of reaction, and he soon learns to treat himself in plenty of time to avoid trouble.

The care of these patients also entails frequent inspection of syringes and a check of the dosage which is actually being given. When the diabetic clinic was first formed, such a check showed that nearly 60% of patients were having a dose at variance with the dose ordered, and these doses ranged from half to double the stated amount. Satisfactory syringes are a problem; the syringe in which the millilitre is divided into tenths is the ideal. Confusion occurs when various strengths of insulin from 20 units to 80 units per cubic centimetre are marked on the syringe; even more confusion occurs when cubic centimetres and minims are present together. For practical purposes, I check a patient's syringe at least twice a year, and always when a new syringe is purchased. Chemists, trained nurses and friends are all only too pleased to give advice on dosage measurement, and it is my sad experience that members of the nursing profession are probably the least reliable in their mathematical calculations.

Control—either initially or when a change of dose is required—is almost always best instituted outside hospital, as we must never forget that our object is to have blood sugar levels within the normal range in the patient who is undertaking his usual occupation and living in his normal environment. One must always be prepared to reduce the dosage by about one-fifth when the ambulant patient is sent home. Too frequently the patient in hospital—and this commonly occurs with children—is well controlled, with exemplary blood sugar levels, only to go home and develop a hypoglycemic coma within the first 24 hours, from the combination of increased activity and excitement. This very occurrence is an outstanding reason against admission to hospital for initial control in the absence of complications. The only patients admitted from the clinic for uncomplicated diabetes are those whose age or whose distance from home precludes their daily attendance at the clinic. Apart from this, some patients are admitted to hospital for two to three days for tests of blood sugar level, but initial treatment as an out-patient is one of the principles of the clinic. This is perfectly feasible in practice if one is prepared to take a little time and effort with the patient in the first week or so, and I am sure it is of enormous value to the patient in nearly every instance.

Together with this initial control, the patient must also be taught the methods of testing the urine for sugar. Benedict's method still holds first place in this respect, as it is a reliable quantitative examination which reveals the presence of sugar in the urine in quantities of about 50 milligrammes per 100 millilitres and upwards. The "Clinitest" method has proved entirely satisfactory, replacing Benedict's, as it is quicker and cleaner and probably cheaper in cost when time is considered. The use of this method has certainly made a vast difference to the amount of time taken in testing urine on clinic afternoons. More recently the enzyme-impregnated paper has been introduced as a means of detecting glucose in the urine, and is entirely satisfactory as a qualitative test for sugar. But it must strongly be stressed that this method has not the least value for a quantitative result (Hunt *et alii*, 1956; Tunbridge *et alii*, 1956).

With regard to the problems raised by diabetes and other illnesses, one must briefly examine pregnancy and surgical operations. At the Queen Victoria Maternity Home, diabetics are concerned in one in 200 deliveries each year. The risk to the mother is negligible, whilst the risk to the fetus is considerable. Congenital abnormalities and the over-sized fetus are problems of their own merit, and one is still faced with an overall fetal mortality of at least 10%. Whether delivery is by Cæsarean section, as in 85% of White's (1952) diabetic mothers treated with massive doses of hormones, or whether delivery is by the normal passages, as in 70% of Pedersen's (1954) series in which no hormones were used, makes little difference. At the Queen Victoria Maternity Home our figures still do not approach this optimum level, and in the last month neonatal death has occurred twice. In both instances the presence of hyaline membrane has been blamed, but the reason for this is not apparent. The need for delivery to be undertaken in the thirty-sixth week is well established, but this is by no means the entire answer. The need for the meticulous care of the mother's diabetes is appreciated, and this has its own special problems in the almost invariable lowering of the renal threshold, which renders fallacious control by estimation of urinary sugar levels. Moreover, even the most careful control throughout pregnancy is no guarantee that an ideal outcome will result. Hoet (1954) holds that the incidence of foetal abnormalities can be reduced if the maternal environment is rigidly regulated throughout pregnancy. He holds that the abnormal maternal environment causes hypertrophy of the islet tissue in the foetal pancreas, and that this is a factor in the high incidence of diabetes in the offspring of diabetic mothers. He states that insulin, in the largest dose tolerable, injected throughout pregnancy, if there is any suspicion of diabetes, will lessen the risk of diabetes in the offspring. It will require many years' observation to prove the validity of this fascinating concept. The most valuable form of care that can be offered to the pregnant diabetic woman is careful and conscientious observation at frequent intervals throughout her pregnancy, at least monthly for the first four to five months, fortnightly to the thirtieth week and then weekly until delivery; early delivery and skilled care of the premature baby are imperative. Actual insulin dosage will vary—in the main it will be increasing—and the type of insulin used will be purely an individual matter. Satisfactory control has been achieved by injecting semi-lente insulin twice daily in all instances. De Costa (1955) summarized the problem by "the four C's": (i) careful diabetic management; (ii) conscientious pre-natal care; (iii) correct timing of delivery; (iv) competent neonatal care.

When a surgical operation is necessary, unless severe ketosis is present, the surgeon can operate as soon as the urgency of the situation dictates. Any surgical intervention, whether it is brief anaesthesia to remove two teeth, or a major procedure such as hysterectomy, may cause a profound disturbance in the control of the patient's diabetes. Suffice it, therefore, if the operation is urgent, to ensure that the patient's urine is ketone-free and that the patient is adequately hydrated. Equally important is it to avoid hypoglycaemia during anaesthesia; but this can be easily controlled by the intravenous injection of glucose. It is essential to change from a long-acting insulin to

ordinary soluble insulin at the time of the operation, and also to cover the immediate post-operative period with soluble insulin. A well-established routine is to inject soluble insulin every six hours during the 24 hours before operation so that the total dose is equivalent to the dose of modified insulin injected before. When possible the surgeon should see that the diabetic patient is first on the list, say between 8 a.m. and 9 a.m. If this is so, provided that the control by modified insulin is adequate, there is no point in altering insulin dosage before operation. No dose should be given on the morning of the operation; soluble insulin should be injected every six hours in the first 24 hours or so after operation, with a return to twice a day as soon as normal food intake and bowel function are restored, and then the usual modified insulin before the patient leaves hospital. It must be appreciated that the endocrine disturbance that follows surgical procedures may take three months or so to return to normal, and during that time the control of diabetes will be liable to wide fluctuation.

Before we examine the more fundamental problems we must consider diabetic ketosis. This is a medical emergency of the highest order, and one must agree with the view that diabetic coma is the result of almost criminal negligence by the doctor, the patient and the relatives (Hunt, 1956). Unfortunately, our records here show that the doctor—the guide to whom the patient turns in time of need—is as frequently an offender as is the patient in initiating the diabetic coma. "I had a bad cold, didn't feel like eating, and doctor said to stop insulin." "Began vomiting two nights ago, and doctor said no more insulin until stomach settled." These are but two extracts from the patient's story, verified in the doctor's letter. Our instructions to the patient specifically cover the occurrence of vomiting, etc., and these instructions should minimize the occurrence of coma.

Why is it that we, as medical advisers, can consistently give the wrong advice? It can be only that we ignore the simplest basic principles: first, the principle that infection increases the requirement of insulin, and that gastrointestinal upsets grossly aggravate the situation by the additional fluid and electrolyte loss they provoke; secondly, the principle that, with any intercurrent illness, evidences of acetoneuria must be sought, and if it is present it must be looked upon as an indication for more strenuous treatment and for more frequent observation. Failure to follow this second principle was the cause of one of our clinic patient's being admitted to hospital in ketosis one month ago. There is no excuse for not testing the urine for acetone. "Acetest" tablets are entirely suitable, and can very easily be carried in one's bag or prescribed to patients for their home use. If Rothera's test of urine is used, one must never forget that salicylates will give the same result even after the urine has been boiled. If ketosis is diagnosed, the administration of 100 units of soluble insulin during the wait for the ambulance may be a life-saving procedure, and in hospital the urgent restoration of fluid and electrolyte deficiencies is as vital as is the need for further insulin. The approach to therapy has been much rationalized after the reports of Nabarro *et alii* in 1952 *et sequentes*, but even so the mortality rate is not inconsiderable, as it was 15% in the last 12 months in the Royal Adelaide Hospital. The plea here is for awareness of the factors which may lead to increased insulin requirements, and of the urgency with which appropriate action has to be taken. Diabetic coma always takes 48 to 72 hours to develop, except in very rare instances, and there is never any reason why the impending disaster cannot be forestalled by frequent observation and appropriate action by the relatives, the patient and the doctor.

Hypoglycaemia is a problem of rapid onset, and is again, on the whole, due to lack of care by both the doctor and the patient. The doctor can help to avoid this condition by frequent review of insulin dosage, and the patient by strict adherence to the regularity of food intake, by early action when symptoms first appear and by discussion with the doctor to try to overcome these reactions. With the use of the modified insulins, behaviour problems are often the most obvious features, ranging from minor mood swings to violent and maniacal episodes, occasionally accompanied

by fits. Often it is the friends or relatives who have to act as the saviour of these people, for, as in the case of alcoholism, the patient's spirit is willing, but the flesh is too weak to act. Here again, an awareness of the problem is more than half the answer.

But let us not take the easy way out and say to the patient: "If you always show a little sugar, you'll never have one of these turns." There are, I admit, some patients for whom one is driven to this as a last desperate resort. But for the majority of patients it is surely a gospel of damnation, which allows poor control to be the yardstick, and which lays the foundation for severe and extensive degenerative changes in the future.

This brings me to the question of complications; the main groups I wish to discuss are those affecting the retina and the kidney, as well as lesions of the feet. In the treatment of all diabetics we must never forget the high incidence of arteriosclerotic changes and their sequelae, but in the retina and the kidney the lesions are more minute and diffuse. Diabetic retinopathy was first described at the end of the last century, and more recently has been widely investigated by Ashton (1950) and by Friedenwald (1950). Clinically, the minute dot haemorrhages are the earliest sign, and these are due to the presence of capillary microaneurysms, usually globular but occasionally saccular in form. These lesions remain visible in a constant position for many weeks or months, after which time they may be absorbed. The presence of these dot haemorrhages in any number is diagnostic of diabetes, and they may occur entirely independently of hypertension and arteriosclerosis; their natural history is to expand and to be associated with more extensive haemorrhage, and overgrowth of retinal vessels. Blindness is their ultimate end result, and 2% of the patients at the clinic suffer from blindness. Apart from rigid control of diabetes, therapy is unrewarding. Vitamins, deep X rays, adrenalectomy and hypophysectomy as therapeutic agents have all been tried, and no certain method of control has been found. Any study of therapeutic measures is greatly hindered by the natural fluctuations that occur in the untreated disorder. Closely parallel to the incidence of retinopathy is the extensive renal lesion first described by Kimmelstiel and Wilson (1936). In its most advanced form it is characterized histologically by the presence of hyaline tufts in the glomerulus, and profound alteration in the basement membrane structure; clinically it is characterized by hypertension, albuminuria and oedema, together with renal failure. This angiopathy is again a reward for long periods of poor control; it is a common feature after 15 years of diabetes, and is almost invariable, in our experience, after 20 years; and renal failure is the unfortunate cause of the death of a number of diabetic patients admitted to the Royal Adelaide Hospital each year. These diabetics have nearly always been quite happily symptom-free for many years. Of course, they have been on a diet and insulin, but questioning them discloses the fact that their diet has been broken fairly often, that usually their insulin was protamine zinc insulin alone, that if they tested their urine it always showed a heavy sugar content, and that they had never had a blood test for the last 10 years or so. Renal failure is one emphatic reason for campaigning against lax therapy. We must have, as our objective, the meticulous control of the patient's blood sugar level, with a view to excluding this dreadful loss of sight and life, the early incidence of which would be greatly lessened by adequate therapy. But although one must adopt such an approach to the patient, there has always been the suspicion that some diabetics will get complications whatever happens, and others will not. This has had some good support recently with the investigations of "brittle" and "stable" diabetes by Alivisatos and McCullagh (1956). These authors suggest that, in spite of the severe problem in management, subjects with "brittle" diabetes are much less likely to suffer from these minute vascular lesions than those with the more readily controlled "stable" diabetes. Conversely, we have all met the patient who has consulted the doctor because of the appearance of one of these complications, the diabetes being discovered only on routine examination. It is of more than passing interest that a clinician as widely experienced as Friedenwald (1950) adopts the following

somewhat negative attitude: "Most investigators have concluded that since there is no evidence that insulin therapy does harm in relation to the retinopathy, it is wise to press, rather than to withhold, the use of insulin."

The third main group of complications I wish to mention is that of lesions of the feet, which are fully described by Oakley, Catterall and Martin (1956). The gangrenous lesion resulting from occlusive arterial disease is unfortunately well known, such ischaemic disasters being common after the age of 50 years. Local digital gangrene may, if treated promptly, be localized and may heal rapidly after excision of the affected toe. The addition of infection raises an acute problem. Unless the exhibition of antibiotics leads to a dramatic improvement within four to six days, below-knee amputation is urgently indicated. Care of the feet, which must be an essential part of the patient's tuition, is the most vital factor in minimizing these lesions.

More fascinating and quite prevalent are the infected ulcerating lesions of the feet as a manifestation of diabetic neuropathy. Neuropathy, as with renal and retinal lesions, is a reward of prolonged, inefficient therapy. It appears as nocturnal burning of the feet, numbness and paresthesia; extensive motor and autonomic involvement follow if it is severe. In the younger age group of patients it is metabolic. But most important is the fact that the awareness of painful stimuli in the feet is greatly diminished. This will allow local trauma to occur to such a degree that tissue necrosis ensues unawares and is usually found only after severe damage has been done. Commonly it is on the sole of the foot, under a horny callus. Blistering occurs with a small extravasation of blood; trauma continues and tissue necrosis occurs; the necrosing area becomes infected; infection tracks deep to involve the metatarsals, and only late in the piece does it discharge to the surface, warning the patient that trouble is afoot. In its extreme form it causes gross destruction of the tarsal bones resembling Charcot's arthropathy.

An example is Mr. A., aged 56 years, who had a cataract removed in October, 1955, at which time diabetic retinopathy was found, but no treatment was undertaken because of an almost normal blood sugar level. Painless blistering resulted after he warmed his feet by a gas fire one night in August, 1956. The fact that any damage had been done to the foot was not appreciated until 24 hours later when, on removal of his sock, a large portion of blistered skin peeled off. In January, 1957, because of a chronic discharging sinus, he sought treatment. Conservative surgery was adopted with the removal of two metatarsals, and we are hoping that further trophic lesions can be avoided.

Whilst a callus is the main trouble, the hot-water bag is another dangerous offender.

Recently a similar lesion occurred after a cataract operation in a woman, aged 56 years. She had had a penetrating ulcer on the third toe for three or four months, but its true nature was unsuspected. Post-operative glycosuria was found on the fourth and fifth days, and when the feet were examined on the sixth day a large blister was found on the tip of the great toe. The fasting blood sugar level was 250 milligrammes per 100 millilitres. Pain, position and vibration sense were lost in both feet, whilst the arterial supply of blood was excellent. This lesion must be looked upon as a pressure necrosis resulting from the weight of the bedclothes on a patient suffering from severe neuropathy.

Two vital points stand out here. First one must beware of the possibility of neuropathy leading to trophic lesions; secondly, as these feet almost invariably have an excellent blood supply, removal of the precipitating trauma and rest will result in rapid recovery, particularly of the superficial lesions such as this last one. Also, when bone infection has occurred, the use of restricted surgery is indicated.

The search for a better control goes on, and in the last few years the oral agents have again had a great deal of publicity. Carbutamide, which was recently heralded as the panacea, has been withdrawn from use by its manufacturers on account of toxic side-reactions. That it is effective in certain instances there is no doubt, but, as has been pointed out by authors in the United Kingdom, in the United States and from the Alfred Hospital, Melbourne (Downie *et al.*, 1957), its mode of action is as yet uncertain—presumably by some interference with hepatic

function—and the long-range results of this are unknown. However, its relative, tolbutamide, has recently been released for general use in the United States, but there are rigid criteria by which the indications for its use are judged. The most recent reports available cover its use in some 5000 cases for a period of six to 15 months, with satisfactory results. Undoubtedly this drug is a step forward, but more time is still required to evaluate its full effect, and to determine whether any toxic reactions in the later periods will operate against its use. Of equal importance in its overall practice is whether this drug will in any way minimize the occurrence of complications.

Lest we lightly accept these new drugs with uncritical thought, it would be wise to reflect on the views propounded by E. M. Allen (1956):

Clinically I view the Blood sugar as the most delicate index of the general metabolic disorder. I also insist that a standard of normality need not be arduous for patient or doctor if both are in earnest. By adhering to it, I claim a record of 40 years without a diabetic complication in a cooperative patient. I, therefore, hold that every complication is the fault of either the doctor or patient. I am glad to be recorded as the first and most consistent upholder of this absolute doctrine, which is increasingly supported by the trend of statistics showing that the supposed constitutional factor shrinks as control improves. I invite confirmation by every doctor who will search into his records and verify that complications are regularly preceded by long and important abnormalities in blood sugar levels. Therefore, I am unwilling to abandon the standard of normal blood sugar for the mere convenience of oral medication.

This forthright opinion is backed by profound experience, and bears constant consideration.

Finally, it is obvious that we must strive to the utmost to keep our diabetic patients healthy with their blood sugar levels within the normal range.

As medical men, we must be able to impress upon the patient that it is he who has to live with his disability; that it is by his own efforts that he can continue to live a healthy life, provided that he is given correct advice; and that it is only by constant endeavour on the part of both the doctor and the patient that the best results will be obtained.

References.

ALVISATOS, J. G., and McCULLAGH, E. P. (1956), "Stable and Brittle Diabetes", *Am. J. Med.*, 21: 344.

ALLEN, E. M. (1956), "Panel Discussion on Sulfonyl-Ureas", *Diabetes*, 5: 371.

ASHTON, N. (1950), "The Pathology of Retinal Microaneurysms", "Concilium ophthalmologicum Britannia (Acta XVI)", 1: 411.

DE COSTA, E. J. (1955), "Diabetes and Pregnancy", *Obst. & Gynec.*, 5: 401.

DITZEL, J., WHITE, P., and DUCKERS, J. (1954), "Changes in the Pattern of the Smaller Blood Vessels in the Bulbar Conjunctiva in Children of Diabetic Mothers", *Diabetes*, 3: 99.

DOWNIE, E., BORNSTEIN, J., and HUDSON, B. (1957), "Hypoglycaemic Sulphonamides in the Management of Diabetes Mellitus", *Australasian Ann. Med.*, 6: 105.

FRIEDENWALD, J. S. (1950), "Diabetic Retinopathy", *Am. J. Ophthalm.*, 33: 1187.

HEALE, T. A. E. (1957), "The Present-day Use of Insulins in the Treatment of Diabetes Mellitus", *M. J. AUSTRALIA*, 1: 665.

HOBST, J. P. (1954), "Carbohydrate Metabolism During Pregnancy", *Diabetes*, 3: 1.

HUNT, B. A. (1956), personal communication.

HUNT, J. A., GRAY, C. H., and THOROGOOD, D. E. (1956), "Enzyme Tests for the Detection of Glucose", *Brit. M. J.*, 2: 586.

JACKSON, W. P. U. (1955), "A Concept of Diabetes", *Lancet*, 2: 625.

JOHN, H. J. (1950), "Prediabetics: What Becomes of Them?", *Am. J. Digest. Dis.*, 17: 219.

KIMMELSTIEL, P., and WILSON, C. (1956), "Intercapillary Lesions of the Glomeruli of the Kidney", *Am. J. Path.*, 12: 83.

NABARRO, J. D. N., SPENCER, A. G., and STOWERS, J. M. (1952), "Treatment of Diabetic Ketosis", *Lancet*, 1: 983.

OKLEY, W., CATTERALL, R. C. F., and MARTIN, M. M. (1956), "Etiology and Management of Lesions of the Feet in Diabetes", *Brit. M. J.*, 2: 953.

PEDERSEN, J. (1954), "Fetal Mortality in Diabetic Pregnancies", *Diabetes*, 3: 199.

ROOT, H. F., JOSLIN, E. P., WHITE, P., MARBLE, A., and BAILEY, C. C. (1948), "Treatment of Diabetes Mellitus", *Lea & Febiger*.

TUNBRIDGE, R. E., PALEY, R. G., and COULSON, D. (1956), "Enzyme Test for Glycosuria", *Brit. M. J.*, 2: 588.

WHITE, P. (1952), "Pregnancy Complicated by Diabetes", *Am. J. Obst. & Gynec.*, 64: 402.

WHITE, P., DUCKERS, J., and KOSHY, P. (1953), "The Management of Pregnancy Complicating Diabetes and of Children of Diabetic Mothers", *M. Clin. North America*, 37.

CALORIMETRY: II. CLINICAL APPLICATION IN PERIPHERAL VASCULAR DISEASE.

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STEWART (1911) was the first to use the principle of calorimetry—that is, determination of the heat released by a hot object—by measurement of the rise in temperature produced in surrounding fluid, as a method for estimation of blood flow through a part of the human body. Calorimetry used for this purpose is applicable particularly to the terminal parts of limbs, especially the hands, although it may be used for the foot or for individual digits (Mendowitz, 1954). Greenfield and Scarborough (1949) described an improved calorimeter for the hands, which was modified slightly by Barnett and Wigley (1953), who critically assessed the method and the precautions necessary in its use.

Calorimetry has been used from time to time as a research method—for example, by Pickering (1936) in investigation of the peripheral resistance in arterial hypertension—but has not found wide clinical use in the assessment of patients with peripheral vascular disease. It is our purpose in this paper to describe our observations on heat elimination measured by calorimetry in a series of "control subjects" and of patients with vascular disturbance of the hands, and to discuss the value of calorimetry as a diagnostic procedure.

Material.

The control subjects comprised 44 persons (26 males and 18 females) who were normal people (students, laboratory workers), or patients with a non-vascular disease who were not severely hypertensive. The ages ranged from 14 to 72 years. For the purpose of this paper, patients with a disease (such as severe diabetes or severe hypertension) which might lead to vascular disorder and those with any marked cardiac abnormality which might lead to an abnormal cardiac output are excluded.

The patients with vascular disturbance comprised 35 persons (nine males and 26 females). They were referred because of ischaemic symptoms (Raynaud's phenomenon, severe coldness, digital gangrene) of the hands. Their ages ranged from 21 to 70 years. The clinical diagnoses are shown in Table II.

Method.

Calorimetry was performed by the method described by Barnett and Wigley (1953). At the beginning of an estimation the temperature of water in the calorimeter was between 27° and 28° C., and it did not usually rise by more than 2° C. during an experiment. Most investigations were conducted in autumn, winter or spring with a room temperature varying from 22° to 25° C. The patient lay on a bed or sat on a chair with one hand immersed in water in the calorimeter to the level of the radial styloid process.

In each instance the "resting" heat elimination was measured first. After this the heat elimination was determined during a "reflex hyperaemia" test, in which heat is applied to another part of the body. This is believed to produce an increase in blood flow in the non-heated member from release of sympathetic nervous tone; no effect is produced in sympathectomized hands. In some of the early investigations heat was applied by means of an electric cradle over the trunk; but in most cases heating was produced by the immersion of one hand and forearm in water at 44° C. for at least 20 minutes. The oral temperature before and after heating was recorded, and usually rose by approximately 0.6° C. (1.0° F.).

In most patients the state of the digital vessels was assessed by an arterial occlusion reactive hyperemia test as described by Lewis and Pickering (1953). In this the

TABLE I.
Frequency Distribution of Heat Elimination in Control Subjects.

TABLE IA.
Subdivided According to Sex.

Heat Elimination (Calories per 100 Millilitres per Minute.)	Subjects.		Total.
	Male.	Female.	
Resting :			
0+	2	1	3
10+	9	7	16
20+	3	4	7
30+	5	2	7
40+	4	0	6
50+	0	0	0
60+	2	0	3
70+	0	1	1
80+	1	1	2
Total	26	18	44
During reflex hyperemia :			
30+	3	1	4
40+	5	1	6
50+	3	1	4
60+	3	1	4
70+	5	4	9
80+	0	2	2
90+	3	2	5
100+	1	1	2
110+	1	0	1
140+	0	1	1
Total	26	18	44

TABLE IB.
Subdivided According to Age Group.

Heat Elimination (Calories per 100 Millilitres per Minute.)	Age Group (Years).			Total
	10 to 29.	30 to 49.	Over 50.	
Resting :				
0+	3	0	0	3
10+	5	6	5	16
20+	4	2	1	7
30+	3	1	3	7
40+	2	4	0	6
50+	0	0	0	0
60+	1	2	0	3
70+	0	0	0	0
80+	1	1	0	2
Total	10	16	9	44
During reflex hyperemia :				
30+	1	1	2	4
40+	0	4	2	6
50+	2	3	3	8
60+	1	2	1	4
70+	5	3	1	9
80+	2	0	0	2
90+	3	2	0	5
100+	4	0	0	4
110+	0	1	0	1
140+	1	0	0	1
Total	19	16	9	44

hands are immersed in water at 35° C. for 10 minutes, and then elevated to empty the veins; arterial occlusion cuffs are applied to the arms and then the hands are again immersed in water of the same temperature for a further five minutes. The arterial occlusion cuffs are then rapidly

deflated in turn. A delay beyond five seconds in flushing of the tips of one or more fingers is taken as evidence of some structural occlusion of digital arteries. In some instances brachial arteriography was also performed and the site of the obstruction demonstrated.

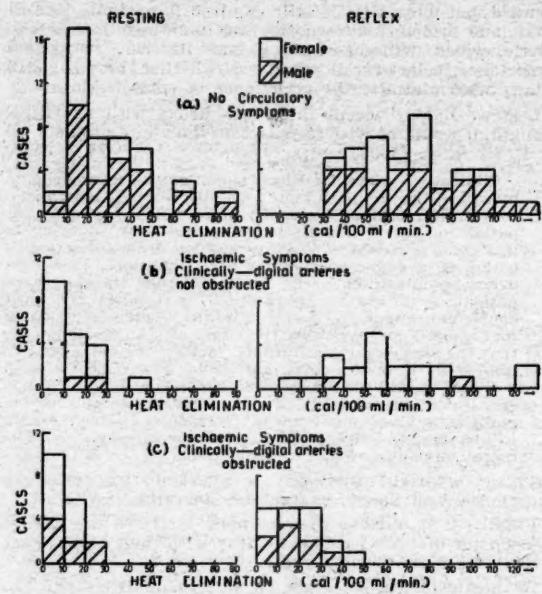


FIGURE I.
Heat elimination—resting and during reflex heating : (a) in subjects without circulatory symptoms; (b) in patients with ischemic symptoms of hands, but without clinical evidence of structural obstruction of digital arteries; (c) in patients with ischemic symptoms of hands and with clinical evidence of structural obstruction of digital arteries.

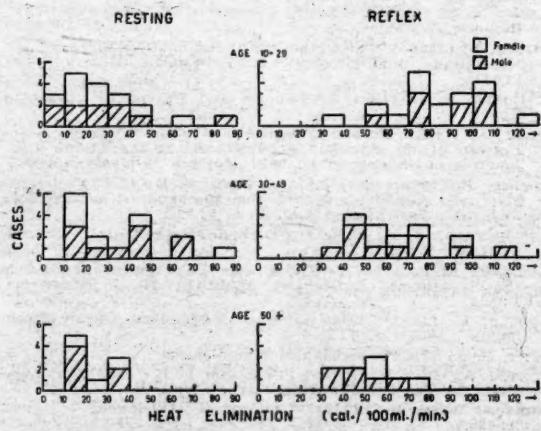


FIGURE II.
Heat elimination, resting and during reflex heating in normal subjects, subdivided broadly according to age groups.

Results.

Comparison of Two Methods of Producing Reflex Hyperemia.

In the early stages of the investigation the resting heat elimination and that following reflex heating was noted in six subjects on two different days. On one occasion

reflex heating was produced by the use of an electric cradle applied over the trunk, and one the other by immersion of one hand and forearm in water at 44° and 45° C. In no instance did the heat elimination obtained after heating the trunk with an electric cradle exceed that produced by immersion of a hand and forearm. Since the latter method is less cumbersome and can be used with the patient sitting, it was employed in all subsequent investigations.

Heat Elimination in Normal Persons.

The resting heat elimination for normal persons ranged between 4 and 86 calories per 100 millilitres per minute, with a mean of 29.3 calories per 100 millilitres per minute (mean for males, 29.3; for females, 29.2). The heat elimination following reflex heating ranged between 31 and 141 calories per 100 millilitres per minute, with a mean

of digital arteries, and 18 hands (of 16 patients) were regarded as having evidence of structural occlusion. Clinical diagnoses and heat eliminations in these patients are shown in Table II. In the patients with no clinical evidence of structural occlusion of digital arteries, the resting heat elimination ranged from 7 to 45 calories per 100 millilitres per minute, with a mean of 12 calories per 100 millilitres per minute, and the heat elimination during reflex heating

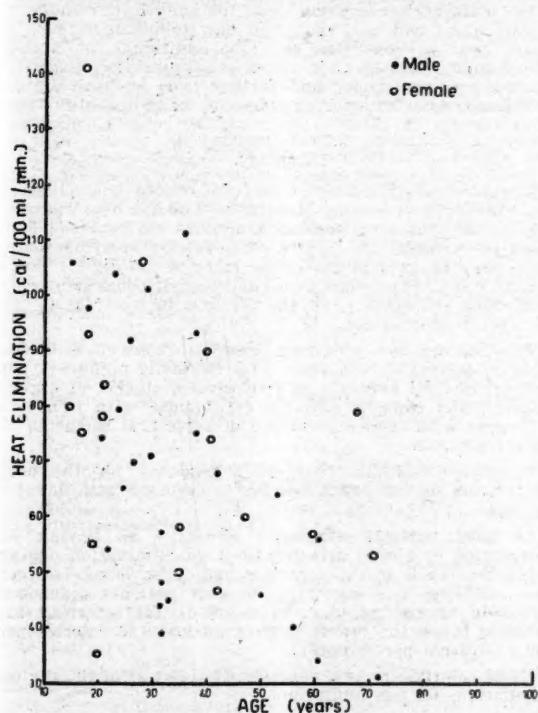


FIGURE III.

Heat elimination during reflex heating, plotted against age of patients.

of 70 calories per 100 millilitres per minute (mean for males, 57.9; for females, 73.1). Usually a severalfold rise in the heat elimination followed reflex heating. In a few instances this did not occur, and occasionally there was a slight fall. In these cases the resting heat elimination was high. Tables Ia and Ib show the frequency distribution of the various heat eliminations (based on subdivisions of 10 calories per 100 millimetres per minute) for the control group, subdivided according to sex and age. The data are represented graphically in Figures I (upper part), II and III. These tables and figures show (i) that there is no striking difference between the heat eliminations in males and females, (ii) that there is no apparent difference between the resting heat eliminations with age, and (iii) that there is a tendency for the heat elimination during reflex hyperaemia to be highest in young persons.

Heat Elimination in Persons with Digital Ischaemia.

On the basis of the arterial occlusion reactive hyperaemia test (described earlier in this paper), 20 hands (of 19 patients) were regarded as having no structural occlusion

TABLE II.
Basic Data, Diagnosis and Heat Elimination in Patients with Digital Ischaemia.

Patient.	Age. (Years.)	Sex.	Diagnosis.	Heat Elimination. (Calories per 100 Millilitres per Minute.)	
				Resting.	During Reflex Heating.
No Clinical Structural Occlusion of Digital Arteries.					
1	33	F.	Raynaud's disease.	45	139
2	32	F.	Raynaud's disease.	7	89
3	29	F.	Raynaud's disease.	8	82
4	31	F.	Raynaud's disease.	6	57
5	61	F.	Raynaud's disease.	7	29
6	49	F.	Raynaud's disease.	3	39
7	48	F.	Raynaud's disease.	7	57
8	28	F.	Raynaud's disease.	17	133
9	37	F.	Raynaud's disease.	8	66
10	21	M.	Raynaud's disease.	18	99
11	38	M.	Raynaud's disease.	22	37
12	46	F.	Raynaud's disease.	5	64
13	62	F.	Raynaud's phenomenon (? cause).	10	47
14	48	F.	Raynaud's phenomenon.	7	57
15	32	F.	Raynaud's phenomenon and acroparesthesia.	22	75
16	42	F.	Raynaud's phenomenon and scleroderma: Right... Left...	8 11	68 39
17	48	F.	Raynaud's phenomenon and scleroderma.	13	52
18	60	F.	Raynaud's phenomenon and scleroderma.	11	16
19	52	F.	Raynaud's phenomenon and scleroderma.	12	32
Clinical Structural Occlusion of Digital Arteries.					
20	53	M.	Scleroderma (localized).	2	3
21	52	M.	Scleroderma (localized).	9	15
22	42	M.	Scleroderma (localized).	7	32
23	60	M.	Scleroderma (localized).	10	15
24	52	F.	? Early scleroderma (localized).	16	33
25	42	F.	Scleroderma (widespread).	6	6
26	48	F.	Scleroderma (widespread).	4	10
27	47	F.	Scleroderma (widespread).	6	22
28	47	M.	Scleroderma (widespread).	23	18
29	36	M.	Scleroderma (widespread).	15	25
30	34	M.	Scleroderma (widespread).	22	22
31	70	F.	Atherosclerosis, thrombosis of digital arteries: Left... Right...	8 14	22 18
32	48	M.	Digital arterial occlusion of obscure cause.	16	23
33	50	F.	Digital arterial occlusion of obscure cause.	10	41
34	54	M.	Digital arterial occlusion of obscure cause.	5	8
35	43	F.	Digital arterial occlusion of obscure cause: Left... Right...	9 7	9 5

ranged from 29 to 139 calories per 100 millilitres per minute, with a mean of 63 calories per 100 millilitres per minute. In the patients with clinical evidence of structural occlusion of digital arteries, the resting heat elimination ranged from 2 to 23 calories per 100 millilitres per minute, with a mean of 10 calories per 100 millilitres per minute, and the heat elimination during reflex heating ranged from 3 to 41 calories per 100 millilitres per minute, with a mean of 18 calories per 100 millilitres per minute. Table III shows the number of patients with various heat eliminations, based on subdivisions of 10 calories per 100 millilitres per minute (for comparison with Table I for control subjects). The lower part of Figure I shows the frequency distribution of the various heat eliminations in the patients

(for comparison with the corresponding distribution for control subjects—Figure 1, upper part).

The tables and figures show that in both groups of patients with evidence of digital vascular disease the resting heat elimination is commonly below 10 calories per 100 millilitres per minute, whereas in control subjects it is rarely in this range. However, there is considerable overlap in the 10 to 30 calories per 100 millilitres per minute range. In patients without evidence of obstruction of digital arteries, the heat elimination during reflex hyperaemia is usually in the normal range (over 30 calories per 100 millilitres per minute); in those with evidence of obstructed arteries it is usually below 30 calories per 100 millilitres per minute.

TABLE III.
Frequency Distribution of Heat Elimination in Hands of
Patients with Digital Vascular Disease.

Heat Elimination. (Calories per 100 Millilitres per Minute.)	Hands.	
	Without Clinical Structural Occlusion. (Group A). ¹	With Clinical Structural Occlusion. (Group B). ²
Resting:		
0+	10	10
10+	5	6
20+	4	2
30+	0	
40+	1	
50+	—	
60+	—	
70+	—	
80+	—	
Total	20	18
Reflex heating:		
0+	—	5
10+	1	5
20+	1	5
30+	3	2
40+	2	1
50+	4	—
60+	2	—
70+	2	—
80+	2	—
100+	0	—
110 and over	2	—
Total	20	18

¹ There were 10 patients in the group A, but in one patient both hands were examined, a total of 20 hands.

² There were 16 patients in group B, but both hands were examined in two patients, a total of 18 hands.

Discussion.

It is seen that the normal range of heat elimination from the hand, both resting and after reflex heating, is very large. Although there is no apparent change in the resting heat elimination with age, there is a tendency for the heat elimination during indirect heating to decrease with increasing age. This lends support to the finding of Lewis (1938) that the intima of digital arteries becomes thicker and in consequence the lumen narrower with increasing age.

The resting heat elimination tends to be low in both types of digital vascular disease, but the overlap between the values found in patients and control subjects is such that this determination has little value in an individual case.

Most patients without clinical evidence of structural digital artery obstruction have a heat elimination during reflex hyperaemia within the normal range; in most patients with clinical evidence of blocked arteries this is below normal. The test used clinically as a criterion of blocking of arteries—the time for flushing of tips of digits after release of arterial occlusion—is based on the state of the

main digital arteries, and it is possible that the few patients in whom this time was normal, but in whom the heat elimination was low, had structural changes in small vessels. In a few patients with clinical evidence of blocked arteries the heat elimination during reflex hyperaemia was normal. This may be explained by the fact that in hand calorimetry the whole hand is immersed in water, and poor heat elimination from some fingers may sometimes be compensated for by good heat elimination from the others. The findings from calorimetry must therefore be interpreted in the light of other features. Theoretically it would be preferable to determine the heat elimination from individual digits, but this is technically difficult.

Hand calorimetry can be performed by a technician with little previous training and gives an over-all picture of the condition of the digital arteries. The results from this investigation cannot always be predicted from the clinical reactive hyperaemia test (which depends on the condition of the main digital arteries), and the quantitative index of resting blood flow and the blood flow following release of sympathetic nervous tone provides additional interesting information. However, it must be appreciated that the method has limitations, and further tests such as digital plethysmography or arteriography may be indicated in some cases.

Summary.

Measurement by calorimetry of the resting heat elimination (an index of resting blood flow) and the heat elimination during reflex hyperaemia (an index of the blood flow when the arteries are dilated after release of sympathetic tone) may be used to assess the state of the digital circulation. Reflex hyperaemia is produced most conveniently by immersing the other hand and forearm in water at 44° to 45° C. for 20 minutes.

The findings are presented from 44 "control" subjects, from 19 patients (20 hands) with ischaemia of fingers but without clinical evidence of structural occlusion of digital arteries, and from 16 patients (18 hands) with ischaemia of fingers with clinical evidence of structural occlusion of digital arteries.

In control subjects there is a tendency for the heat elimination during reflex heating to decrease with advancing age.

In most patients diagnosed clinically as having no obstruction of digital arteries, the heat elimination during reflex heating is in the normal range (over 30 calories per 100 millilitres per minute); in most patients diagnosed clinically as having obstruction of digital arteries, this value is below the lower limit of normal (30 calories per 100 millilitres per minute).

Hand calorimetry is a valuable, simple test of the digital circulation, but has limitations.

Acknowledgements.

Our thanks are due to various resident medical officers of the Alfred Hospital and technicians of the Baker Medical Research Institute, who helped in the calorimetry, and to Dr. T. E. Lowe, Director of the Baker Medical Research Institute, for advice and encouragement.

References.

- BARNETT, A. J., and WIGLEY, G. R. (1953), "Calorimetry: A Method of Estimating Peripheral Blood Flow", *M. J. AUSTRALIA*, 2: 326.
- GREENFIELD, A. D. M., and SCARBOROUGH, H. (1949), "An Improved Calorimeter for the Hand", *Clin. Sc.*, 8: 211.
- LEWIS, T. (1938), "The Pathological Changes in the Arteries Supplying the Fingers in Warm-Handed People and in So-Called Raynaud's Disease", *Clin. Sc.*, 3: 287.
- LEWIS, T., and PICKERING, G. W. (1933), "Observations upon Maladies in which Blood Supply to Digits Ceases Intermittently or Permanently, and upon Bilateral Gangrene of Digits, Observations Relevant to So-Called Raynaud's Disease", *Clin. Sc.*, 1: 327.
- MENDOLOVITZ, M. (1954), "The Digital Circulation", Grune & Stratton, New York: 60.
- STEWART, G. N. (1911), "Studies on the Circulation in Man. I: The Measurement of the Blood Flow in the Hands", *Heart*, 3: 38.

Reviews.

El Hipnotismo de Hoy. By Galina Solovey and Anatol Millechin. 1957. Buenos Aires: Ediciones "Dyaus". 7½" x 5½", pp. 288. Price not stated.

GALINA SOLOVEY and Anatol Millechin of Uruguay have written in collaboration many papers on hypnotism in the *Journal of Clinical and Experimental Hypnosis*, the *British Journal of Medical Hypnotism*, *El Día Médico Uruguayo* and as chapters in books of comprehensive character. They now publish what they regard as a modern and up-to-date pronouncement on the subject. The authors would have given a more acceptable and certainly a shorter exposition had they devoted less space to assuring the reader that work on this subject in the last 10 years has displaced older and erroneous conclusions. "Libraries are full of books written in a past age, or contemporary books repeating old ideas." Just as the geocentric description of the solar system remained long after Copernicus, so the now discredited opinions of Charcot and others are still to be found in many expositions and criticisms of hypnotism, so the authors contend, hindering the acceptance by the medical profession of the scientific treatment of today. Hypnotism, according to them, is nothing more than a special branch of psychotherapy, and should take its place with ancillary procedures. If psychic states can produce cardiac irregularities, arterial hypertension and ulcers of the stomach and duodenum, then, the authors claim, psychic measures can be used in special cases for prevention or treatment. It would have been better had the authors refrained from accepting as correct the uncritical assurances of many exponents of the method; thus they mention without comment that MacDowell in 1953, in his chapter "Hypnotism in Dermatology", included in the book "Hypnotism in Modern Medicine", confidently asserted that he had effected or seen cures of *alopecia areata*, lichen, pemphigus, acne, pruritus, drug dermatitis, urticaria and warts. Chile, we are informed, was the first country in South America to include hypnotic theory and practice in the medical curriculum. Before this precedent is widely followed, much will have to be done to convince medical practitioners that hypnotism displays the consistency in results which a scientific system should possess.

Aortography: Its Application in Urological and Some Other Conditions. By W. Barr Stirling, Ch.M., F.R.C.S. (Ed.), F.R.F.P.S.G.; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 9½" x 6½", pp. 300, with 155 illustrations. Price: 60s. (English).

This monograph is a well balanced appreciation of the applications of aortography by a urologist who has considerable experience and interest in the technique and applications of aortography. It is printed on good quality paper and well set out, and the reproductions of X-ray films are excellent.

The first section is devoted to the history, anatomy and technique of aortography, its hazards and applications, and certain investigations into pressure factors carried out by the author himself. It is no cursory survey, but a thoughtfully prepared résumé with much useful and practical advice. The chapters following deal with renal anomalies, cysts, neoplasm, hydronephrosis, calculus, tuberculosis, hypertension, hypoplasia and post-operative function. In these the author, with the aid of case histories, has skilfully demonstrated the type of help the ingenious urologist may expect from aortography. Other sections are devoted to diseases of the adrenal glands, obliterative vascular diseases, and bone tumours.

The author dismisses serial cassette changes as an unnecessary adjunct to aortography. Few radiologists would agree with him in this, as in his examples of solitary kidney the film taken in the arterial phase in several of the illustrations was obtained before there was adequate filling of the iliac arteries. It is perhaps unfortunate that he should condemn retrograde femoral catheterization, particularly because, since this book was published, much has been written about selective renal angiography via the femoral artery. It is doubtful whether an amount of one to two cubic centimetres of contrast medium injected intravenously is not an excessive dose for the testing of the patient's sensitivity.

In the section on renal neoplasm, the author states that angiography will provide a definite diagnosis in every case of solid tumour. While this statement is intended to apply to a parenchymal adenocarcinoma, in the experience of many people it is an unacceptable generalization, as the differentiation between a small cyst and a small neoplasm may not be possible.

In all, this book has much to recommend it as a thorough and interesting survey of a useful examination. There is an excellent bibliography, and it should be of interest to both urologist and radiologist.

The Chemistry of Organic Medicinal Products. by Glenn L. Jenkins, Walter H. Hartung, Kenneth E. Hamlin, Jr., and John B. Data; Fourth Edition; 1957. New York: John Wiley and Sons, Incorporated. London: Chapman and Hall, Limited. 9" x 6", pp. 580. Price: \$10.75.

THIS is an up-to-date, accurate review of the important organic substances used as therapeutic agents. It is well provided with structural formulae and references to review articles and original literature. Although the text is heavily biased towards the chemistry of the substances discussed, reference is made to pharmacological properties, to natural sources and in some instances (rather too few) to metabolic changes. A concise review of the antibiotics has been added in this edition, and the very good chapter dealing with stereoisomerism as applied to medicinal chemicals has been brought up to date.

Authors of texts on pharmaceutical chemistry are confronted with the difficult choice of classifying substances according to their chemical properties or into pharmacologically related groups. The text under review uses the former method in the main, with the result that many anomalies arise. Thus the important local anaesthetic lidocaine ("Xylocaine") is not discussed with procaine and the other "ester" type anaesthetics, but in a different section under amides, its correct chemical group. The result is that discussions on constitution-action relationships are often incomplete. Because of chemical differences the vitamins are scattered in several sections, and the oxidation product of adrenaline, adrenochrome, is not discussed with the parent substance, where one might expect to find it. Many instances of diffusion of this nature are in evidence, and a much more coherent text would result if the chemical classification was adhered to less rigidly. Also, one expects to find in a text-book of this nature information about the chemical stability of the substances described under varying conditions of storage and solution, sterilization, etc. Very little discussion of this nature appears—the decomposition of barbiturates in aqueous solution is, for example, not mentioned, and other examples of similar omissions could be pointed out.

However, the text is a well established one, and is a very useful reference for any person seriously interested in organic therapeutic agents. The grouping together of diverse pharmacological agents according to chemical type does at least have a salutary effect upon those who tend to read more into the relationships between chemical structure and pharmacological activity than is good for the imagination.

Anesthesia and Otolaryngology. By Donald F. Proctor, M.D.; 1957. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" x 6", pp. 236, with 33 illustrations. Price: 77s.

In this excellent book, Donald F. Proctor gives in compact form a most lucid survey of the problems involved in the safe and efficient care of patients during ear, nose and throat investigations and operations. Indeed, he goes further, and discusses the significance of these questions in thoracic surgery as well as in the resuscitation of the newborn. His long experience in oto-laryngology, together with four years spent as Director of Anesthesiology at the Johns Hopkins University School of Medicine, amply qualifies him to speak with authority about these frequently interdependent clinical specialities. In making a strong plea for the better recognition of anaesthetists and their difficulties, he insists that they in turn should know more about surgical considerations. Only by mutual understanding and tolerance between their attendants will patients receive maximum benefits, whereas disputation and misunderstanding may well lead to disaster.

Throughout this book there is a repeated emphasis on the imperative need for preserving efficient pulmonary ventilation during the procedures under review, not only to supply oxygen, but also to remove carbon dioxide with its deleterious possibilities. The great value of tracheal intubation is freely acknowledged; but warning is given against any false sense of security that it may encourage in those not sufficiently impressed with the continuing need for assistance to depressed breathing. In this connexion the over-liberal use of narcotic drugs is deprecated, soluble barbiturates given by the intramuscular route being preferred.

The book contains a great number of useful hints, which should be thoroughly appreciated by anaesthetist and surgeon alike. The value of early tracheotomy in many serious cases is emphatically stressed. A recommendation that a combina-

tion of topical analgesia, thiopentone given intravenously and insufflated nitrous oxide and oxygen is suitable for tonsillectomy must be viewed with reserve. Even if it might permit the use of diathermy, this certainly would favour aspiration and consequent lung complications. Frequent mention of the Davis-Crowe gag is hardly complimentary to the late Dr. H. E. G. Boyle, of London. The scope of local analgesia for many endoscopic and other procedures is convincingly set out, while the author's general adherence to standard English must be highly pleasing to British readers.

Combined Textbook of Obstetrics and Gynaecology: For Students and Practitioners. Edited by Dugald Baird, B.Sc., M.D., D.P.H., F.R.C.O.G.; Sixth Edition: 1957. Edinburgh and London: E. and S. Livingstone, Limited. 9 $\frac{1}{2}$ " x 6 $\frac{1}{2}$ ", pp. 948, with 492 illustrations. Price: 95s. (English).

This new edition of this well known British text-book has appeared after a period of seven years and includes much new material. While reducing the volume by some 475 pages, Professor Dugald Baird and his distinguished team of co-authors have packed this book with the essence of their knowledge and experience. It is written primarily for students and general practitioners, and presents in condensed form much of the clinical and statistical research work produced in Britain and Aberdeen, particularly during the last two decades.

In an attempt to cover the widest possible field and yet condense the book into its 936 pages, much detail has been eliminated. For the general practitioner who has already a background of obstetrics and gynaecology, this volume is comprehensive and contains sound teaching and up-to-date information. It is written in essay form and is very readable. The student will find a wider approach to obstetrics and gynaecology than is usually given in undergraduate textbooks, but, being presented with so much information in condensed form, may find difficulty in assimilating the basic principles.

Although in the preface Professor Baird has pointed out the importance of the psychological element in diagnosis and treatment, this chapter has been relegated to the end of the book. It seems a pity that so important a topic should be so placed. The operative sections, in general, give only a guide to follow the principles of the operations described, but insufficient technical details for any operative work.

The book is well produced and illustrated, and is a worthy successor to the previous edition.

Fat Consumption and Coronary Disease: An Evolutionary Answer to This Problem. By T. L. Cleave, M.R.C.P. (Lond.), with a foreword by Percy Stocks, C.M.G., M.A., M.D. (Camb.), F.R.C.P. (Lond.), F.S.S.: 1957. Bristol: John Wright and Sons, Limited. 7 $\frac{1}{2}$ " x 4 $\frac{1}{2}$ ", pp. 40. Price: 5s.

DESCRIBED AS "a basic approach to the prevention and arrest of coronary disease", Surgeon Captain T. L. Cleave, R.N., sees in the genesis of atherosclerosis a departure from the natural appetite for natural fats. He develops the theme that, given full freedom, a healthy appetite will itself dictate the quantity and quality of fat to be consumed; the adult tongue will reject a bitter or unpleasant taste from a substance occurring in the natural environment of the animal, and so protect the organism from a poison. He feels that this protection applies also to cooked food, provided its constitution has not been changed in the process. Saturated fats may become pathogenic in this way, and may even have been made more attractive to the palate, contributing thereby to ultimate atherosclerosis. Captain Cleave indicts arbitrary meals, i.e., meals taken as a guest, and not prepared by the consumer himself, and arbitrary food mixtures, e.g., fried foods, as particularly noxious, since the tongue is not consulted, and good manners lead one inevitably to the hospital or morgue. He considers that processed foods, including chocolate and ice cream, the consumption of which mounts continually, are particularly subtle poisons. Sophisticated eating is the most certain way of digging one's grave with one's teeth, and industrialization leads to unnatural fat consumption and racial suicide, with the sedentary workers disappearing first. All other factors known to modify the incidence of coronary disease, such as sex, age, hypertension, and possibly alcohol and tobacco, play a secondary role, while the natural law of adaptation dominates any local factor, such as mural thrombosis or stress in susceptible vessels. To prevent or arrest coronary disease, therefore, it is essential to eat only natural foods individually desired. One must decide beforehand what it is which one really wishes to eat, as delicious food may arouse a spurious and dangerous appetite.

Such a cult will not prove popular, but will develop character and self-discipline. It should control obesity and gluttony, and in so doing delay the appearance of hypertension and arterial degeneration. The all-important influence of heredity will, however, probably not be denied. Captain Cleave has written an entertaining little monograph, and shows that he has given much thought and rationalization to his hypothesis. His views will be more acceptable to vegetarians and Eskimos than to the food industry.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Chronic Bronchitis Emphysema and Cor Pulmonale", by C. H. Stuart-Harris, M.D. (Lond.), F.R.C.P., and T. Hanley, M.D. (Lond.), M.R.C.P. Written in collaboration with Marjorie Clifton, M.D., Margaret M. Platts, M.D., B.Sc., M.R.C.P., and W. Whitaker, M.D., M.R.C.P.; 1957. Bristol: John Wright and Sons, Limited. 8 $\frac{1}{2}$ " x 5", pp. 256, with 61 illustrations and 41 tables. Price: £2 2s. (British).

From the Department of Medicine, University of Sheffield.

"Protein Chemistry", by Sidney W. Fox and Joseph F. Foster: 1957. New York: John Wiley and Sons, Incorporated. London: Chapman and Hall, Limited. 9" x 6", pp. 472, with many illustrations. Price: \$9.50.

"A balanced treatment of protein chemistry, including the important component subjects of amino acids and peptide chemistry."

"A Textbook of Fractures and Related Injuries", by J. Grant Bonnin, M.B., B.S. (Melbourne), F.R.C.S. (England); 1957. London: William Heinemann (Medical Books), Limited. 8 $\frac{1}{2}$ " x 6", pp. 722, with 775 illustrations. Price: 84s. (English).

The author is consultant orthopaedic surgeon to the Central Middlesex Hospital.

"Radiological Physics", by M. E. J. Young, M.Sc.; 1957. London: H. K. Lewis and Company, Limited. 9 $\frac{1}{2}$ " x 5 $\frac{1}{2}$ ", pp. 378, with 184 illustrations. Price: £2 2s. (English).

Intended for students working for the diplomas in radiology of the Royal College of Physicians and the Royal College of Surgeons or for membership or fellowship of the Society of Radiographers.

"The Dynamics of Anxiety and Hysteria: An Experimental Application of Modern Learning Theory to Psychiatry", by H. J. Eysenck; 1957. London: Routledge and Kegan Paul. Sydney: Walter Standish and Sons. 8 $\frac{1}{2}$ " x 5 $\frac{1}{2}$ ", pp. 326, with 61 illustrations. Price: 32s. (English).

The author is a lecturer in psychology at the Institute of Psychiatry (Maudsley and Bethlehem Royal Hospitals) and Director of the Psychological Department.

"A Short History of Psychotherapy in Theory and Practice", by Nigel Walker, Ph.D.; 1957. London: Routledge and Kegan Paul. Sydney: Walter Standish and Sons. 8 $\frac{1}{2}$ " x 5 $\frac{1}{2}$ ", pp. 200, with illustrations. Price: 25s. (English).

The author traces the development of modern psychotherapeutic methods from Freud and his colleagues down to the modern psychoanalysts, analytical psychologists and group therapists.

"An Introduction to Experimental Surgical Studies", by W. J. Dempster, F.R.C.S.; 1957. Oxford: Blackwell Scientific Publications. 8 $\frac{1}{2}$ " x 5 $\frac{1}{2}$ ", pp. 464, with 72 illustrations. Price: 50s. (English).

The author is Lecturer in Experimental Surgery at the Postgraduate Medical School of London.

"Connective Tissue", edited under the direction of R. E. Tunbridge, Madeline Keech, J. F. Delafresnaye, and G. C. Wood; 1957. Oxford: Blackwell Scientific Publications. 8 $\frac{1}{2}$ " x 5 $\frac{1}{2}$ ", pp. 384, with illustrations. Price: 42s. (English).

A symposium organized by the Council for International Organizations of Medical Sciences.

The Medical Journal of Australia

SATURDAY, MARCH 22, 1958.

MEDICAL CONTRIBUTIONS TO HISTORY AND BIOGRAPHY.

To attempt diagnosis and treatment at a distance of place or diagnosis at a distance of time is contrary to medical tradition. Occasionally in peculiar emergencies (or even as normal practice in remote areas) it may be necessary for humanitarian reasons to learn what is possible concerning a distant patient, and by further use of telephone or radio to suggest appropriate treatment, but this is a task which no doctor regards with pleasure. To diagnose a pathological condition occurring in past time has the added difficulty that, apart from trauma, the cause of the complaint cannot be described in terms conformable with modern usage, and further, the signs and symptoms are presented without any contribution from diagnostic methods since evolved. No historian today accepts Carlyle's dictum that history is but a series of biographies; many great movements involving trade, migration, discovery and conquest have developed independently of outstanding leaders, and often an alleged innovator is merely swimming with the tide. However, it must be conceded that the purely personal can determine the direction and speed of a movement in action or thought. Blaise Pascal's aphorism, "Had Cleopatra's nose been shorter the whole history of the world would have been different", must not be taken too literally; we may venture to question whether the rise of the Roman imperium and the decline of Roman virtue and power would have been affected if the Egyptian queen had never existed. Still, a human being possessing power and capable of leadership can act as a catalyst, not only hurrying up a process already in operation or ripe for introduction, but in a limited manner influencing the direction in which subsequent events take place. It is in this restricted field that medical biography can be of service; as also can the study of great epidemics and famines which affected the population of cities and communities. The condition of society in the Middle Ages cannot be understood unless we keep in mind the fact that disease and winter malnutrition kept population static—there was no pressure of population enforcing emigration or war. When Jenner in 1798 gave the civilized world vaccination, he unconsciously bestowed the manpower for the industrial revolution.

In the attractive department of medical biography there have been but few investigators; one thinks of Cabanès, of France, and Charles MacLaurin, of Sydney, the latter being perhaps the greatest in this field. The complete absence of data obtained by modern methods of examination makes diagnosis in past time highly speculative and often capricious, and the more remote the age, the greater is the uncertainty. One cannot affirm with assurance if leprosy existed in Biblical times; it probably did, but, as Professor Abbie remarked recently,¹ "One wonders how many sufferers from innocent skin complaints were condemned to the misery and isolation inflicted by the label 'leper, unclean'". There is just one epidemic occurring in classical times which can be diagnosed with reasonable certainty—namely, that in the time of Justinian. Although Gibbon's view was that it was caused by heaps of dead locusts, what detail is given strongly suggests bubonic plague. But what of the devastating epidemic under Marcus Aurelius? "Smallpox", say some, but that is a pure conjecture. Also the epidemics in the time of Pericles and Constantine V. When did malaria begin to depopulate Mediterranean countries?

One branch of medical science, ophthalmology, is particularly rich in unanswered queries when we think of those famous personages who suffered from visual defects. Nero's use of an emerald, at least of a green stone, to aid his vision has led to a series of guesses, but we may rule out two of these, one being that the stone acted as a concave mirror, the other that it was a convex lens. Did he look through a hole and so correct astigmatism, or was the improvement purely psychic? Dante tells us that his eyes were weak, but gives not the faintest clue as to the real nature of his disability. What was Milton's blindness? Glaucoma following hypermetropia, say some, but this has not received full acceptance. Lambert Rogers suggests that he had a suprachiasmal cystic tumour.² What was the visual trouble which has robbed us of thirty years of Pepys's lively diary? Was it advanced astigmatism or something more organic? The unocular blindness which was inflicted on Nelson by a blast of pebbles following the impact of a nearby cannon ball was probably retinal detachment, but again certainty is not attainable.

In diagnosing as poliomyelitis the malady which gave a lasting lameness to Walter Scott—his autobiographical comment is "teething trouble"—we are on fairly safe ground; as also with gall-stones which brought on the sudden attack of colic followed by icterus—Scott's description was "cramps in the stomach". Napoleon III must have suffered agonies of pain at Sedan with a large and rough vesical calculus rubbing on an ulcerated bladder with every jolt of his horse. It is, however, when we come to the story of Napoleon I that we find medical historians running riot in dogmatic diagnoses. Professor Mario Vitiello, of Rome,³ in an article entitled "*Le malattie di Napoleone e la sua autopsia*", gives a list of maladies which have been variously ascribed to the great Captain, and which he apparently accepts as correct. In that list we find tertian malaria, tuberculosis of the lung, of the stomach and of the bowel, pleurisy with effusion, persistent

¹ M. J. AUSTRALIA, 1957, 2: 925 (December 28).

² J. Hist. Med., 1949, 4: 468. See also M. J. AUSTRALIA, 1950, 1: 539 (April 22).

³ Minerva Med., 1957 (September 15).

night cough with haemoptysis, tropical hepatitis, tropical enlarged liver and tropical enlarged spleen. Others have added Mediterranean fever, hypopituitarism and frequency of micturition—but how caused? It is a little amusing to find that of the two diseases which lay opinion credits Napoleon with possessing we can with certainty dismiss both. One is epilepsy, for the existence of which there is not one scintilla of evidence; the other is cancer. E. Kalima,¹ of Helsinki, published an article, "De quelle maladie est mort Napoleon I", in which he convincingly pointed out that Napoleon suffered from perforating ulcer of the stomach and not cancer. This contention has been subjected to a critical study based on vast clinical and operative experience by Sir Hugh Devine and declared to be correct. The ordinary man in the street will ask how it was that Napoleon, if he suffered from all the ailments listed by Professor Vitiello, was able to display an amazing bodily activity; how it was that he was able to march alongside his soldiers over the scorching sands of Egypt, over the snowy passes of the Alps, over the ice of Russia and the clogging mud of Poland; how he was able to bivouac without shelter and give an example to his soldiers. Marlborough after battle suffered from severe headaches, from which he found relief by copious blood-letting. Napoleon was content with a hot bath and was able to turn his brain with unaffected strength to all sorts of problems presented by his European empire—thus after Borodino he dictated full details concerning the construction of the Opera House in Paris. The man in the street will assuredly have good sense on his side; Napoleon must have enjoyed particularly good health through most of his career to have done what he did.

Our conclusion then is that the study of epidemics and of personal maladies can be of some service in illuminating problems presented by history, but the diagnostician must walk warily and be ever conscious of the liability to err and of the danger of letting enthusiasm take the place of knowledge.

Current Comment.

FAT CONSUMPTION AND CORONARY DISEASE.

It ate the food it ne'er had eat.

—*The Rime of the Ancient Mariner.*

THE great efforts made everywhere to elucidate the causes of atheroma and particularly of occlusive coronary atheroma leave most doctors who try to assimilate them with mental indigestion—and this very often despite a lively personal interest in the subject. The subject is by no means new to these columns, but interest in it is unabated. The key to prophylaxis is presumably aetiology, yet the more one learns of this the more it seems that there is to learn. Our patients, excited by each new discovery reported in the daily papers or the popular magazines, prod us with a host of questions, of which none are more difficult than those about the relationship between fat intake and coronary disease. One can recall many such questions from patients with acute and untrammelled minds, who have a fair idea of what atheroma is, and one can also recall the difficulty of framing simple yet satisfactory answers:

Is atheroma composed of fat? Not fat exactly; it is mostly a lipoid substance called cholesterol.

What is a lipoid? It is a fat-like substance, but chemically not a fat.

In last Sunday's paper they called it lipid: is that the same? Very much; a lipoid is a lipid, but a lipid is not necessarily a lipoid.

Is lipoid manufactured in the body or is it taken in with the food? Both.

If it has dietary sources, what are they? Egg yolk, liver, kidney, brains and animal fat (cream, butter and meat fat).

Well, why not cut all these things out of the diet, so that no cholesterol or any ingredient of it enters the system? Remember that cholesterol is a necessary part of every cell in the body and that, even if you starve yourself, you "live on your own fat", which is animal fat, of course, and all the cholesterol required is formed in the process and may rise to a quite high level in the blood.

The writer in last Sunday's paper said that eating only unsaturated fats would lower the level of cholesterol in the blood, but saturated fats did the opposite: how can you tell which is which of these fats? The layman can't; but corn oil, sunflower-seed oil, sardine oil and butter fat are all largely unsaturated.

Can I buy corn oil? Yes; but wait a minute; are you satisfied that bringing down your blood cholesterol level a bit, assuming that corn oil will do that, will prevent atheroma if you haven't yet got it or lessen it if you have?

I obviously can't express an opinion. What's the answer? That's what the doctors want to know.

We answer our patients, and it is easy to show that we know more than they do; but perhaps we still cannot see the wood for the trees, which become ever more numerous.

Thus we may turn with readiness, tinged perhaps with scepticism, to a new and "basic" approach to the prevention and arrest of coronary disease, which claims to answer the problem of the relationship between fat consumption and coronary disease on evolutionary grounds. This is the approach of T. L. Cleave, in a book reviewed elsewhere in this issue. Cleave builds his thesis on Darwin's law of adaptation, from which it follows that every living organism must be perfectly adapted to its natural environment. With its senses, evolved down the ages, to guide it, an organism can avoid what is harmful and eat what is good for it; but only so long as its senses are exercised on naturally occurring substances. The human race may safely rely upon its senses of taste and smell even with cooked food; for, according to Cleave, man has been cooking food for some two hundred thousand years and has become by evolution considerably adapted to it, as the study of ancient and modern skulls shows. However, the senses may be led badly astray by the presentation of refined and concentrated foods, which may lead to the harmful over-consumption of carbohydrates, and by the consumption of "arbitrary meals" and "arbitrary food mixtures", which very frequently leads to the consumption of fat greatly in excess of any need or instinctive desire or even taste for it. It is to dietary excesses of this general nature that Cleave seeks to attribute the increased incidence of coronary atherosclerosis in our civilization, and the steps of his argument are reasoned with much cogency. Whether everyone will find them convincing is another matter.

It has been supposed that the great variations in mortality from coronary disease among Western countries having a similar high intake of fat dispose of any proposition that the total consumption of fat is the critical causative factor. Cleave argues that such variations do not dispose of his proposition that unnatural fat consumption is the critical factor and that, indeed, such variations would be a strong probability if it were the factor: what is natural for the Eskimo in his natural habitat would be unnatural in Chicago. He points to industrialization, through its augmenting food sophistication, as one of the biggest causes of unnatural fat consumption. A comparison of the incidence of coronary disease and of circumstances favouring particular food habits in different countries and occupation groups shows unnatural fat consumption running through "like a golden thread". In the final chapter setting out in detail the dietetic prevention and arrest of coronary disease, the

¹ *Acta chirurg. scandinav.*, 1932, 77.

reader is advised to eat natural foods and to decide before each meal what it is that he really wishes to eat. No doubt such advice may be passed on from doctor to patient with better hope of its being understood than any general prohibition or limitation of fats or attempts to discriminate between fats of one kind of molecular structure and fats of another.

There is a considerable body of opinion which does not accept the notion that coronary disease is related to a high fat intake. M. Friedman and R. H. Roseman,¹ for instance, who found that American women of the upper economic strata eat as much fat as their husbands, have sought to show that their relative immunity from coronary disease is not due only to their sex. They have also related the intake of fat to the incidence of coronary disease in the American male and conclude that the two are unrelated; they speak of "the atherogenic potential of socioeconomic stress", peculiar to and characteristic of the middle and upper class male of Western society. Cleave would doubtless answer this by relating socio-economic stress to a compulsion to partake of arbitrary meals. Whether or not Cleave's views on the causes of coronary disease later prove to be erroneous, his dietary advice cannot be otherwise than pleasant and salutary; for no basic food is forbidden and no natural desire for food is thwarted. However, it might lead to greater expense, because it is one of the paradoxes of our times that natural foods often cost more than sophisticated foods. Also some bad habits might be difficult to break.

INTRAVENOUS TRANSFUSION OF BONE MARROW.

THE use of radiation, in particular whole body radiation, and of drugs of the melamine type in the treatment of leucæmias and other forms of diffuse cancer can lead to practically complete destruction of bone marrow with fatal results. Experiments with rats, dogs and monkeys, carried out by a number of different observers, have shown that after a lethal dose of radiation the destroyed bone marrow may be repopulated by intravenous infusion of cellular suspensions of marrow taken from healthy isologous and homologous donors, and that the marrow cells can be kept effective for some time if frozen in glycerol to -80° C. Man does not react in exactly the same way as other animals to intense irradiation, so one cannot assume that he will react in the same way to marrow infusion. There are many difficulties in experimenting with man in this way, but E. D. Thomas, H. L. Lochte, Wan Ching Lu and J. W. Ferrebee² consider that "in an atomic age, with reactor accidents, not to mention stupidities with bombs, somebody is going to get more radiation than is good for him", and it is high time that someone should see whether marrow cell injections might be useful in man. Their investigations are of a preliminary nature to see whether marrow injections can be given with safety to man. The human bone marrow was obtained from fetal and adult cadavers, from ribs removed at surgery, and from aspiration biopsy material from the ilium of donors under anaesthesia. The marrow was passed repeatedly through a stainless steel screen and broken into a smooth, cellular suspension, and, as a rule, the fat was removed by centrifugation. The cells, resuspended in tissue-culture fluid and serum, were administered intravenously. Marrow cells prepared in this way and mixed with glycerol were kept in good condition at -80° C. for three weeks. Injections were given to several patients in the last stages of conditions such as cerebral haemorrhage and carcinoma, to see if there were any untoward results (such as pulmonary emboli and histological changes) seen *post mortem*, but none were found. Patients with leucæmia or myeloma, treated with radiation, reacted in the same way to infusion and showed no successful homograft. Apparently there was not sufficient impairment of the immune response by the radiation administered. A

similar result was obtained with a patient receiving nitrogen mustard. One patient suffering from lymphatic leucæmia, treated with whole body irradiation, did show evidence of a temporary "take" of the homograft as indicated by the appearance of red cells of the donor type in the blood for several days. Probably the radiation given caused a temporary impairment of immune response to the donor marrow.

The experiments here outlined show that human bone marrow can be collected and stored in significant quantities and administered with safety. None of the patients studied had had a sufficiently large dose of radiation or chemical to effectively destroy the bone marrow and the body's immunity to foreign marrow. The considerable success gained by marrow infusion in laboratory animals and the results reported in this paper justify further trial.

THE ERADICATION OF YAWS.

Yaws can be eradicated from all tropical areas of the world, including Africa, within the next ten years, according to a progress report submitted to the Executive Board of the World Health Organization recently. By the end of this year, half of the 200 million people exposed to this hideous tropical disease will have been examined and about 25 million will have received injections of long-lasting penicillin able to suppress the infection. Total success will have been achieved when the remaining 100 million people living in yaws areas have been examined, and those infected—estimated at 25 million—successfully treated. The job is expected to take 10 years, since most of the yaws victims remaining live in Africa, where mass health campaigns are difficult to conduct because of distance, scattered populations, lack of funds and other factors.

The largest single campaign at present is that in Indonesia, where more than 23 million people had been examined and 3.6 million treated by the end of 1956. In the course of re-surveys, 31 million were examined and 1.4 million treated. Another large campaign is taking place in Thailand, where approximately 20 million people had been examined by the end of 1957. Smaller campaigns are in operation in Malaya, in Laos and in the Pacific Islands (Fiji, Solomon Islands, New Hebrides) with encouraging results. Data from Western Samoa showing the great regression of yaws, approaching total eradication, indicate that in the first campaign 11% of the people examined were suffering from yaws, in the first re-survey only 0.06%, and in the second 0.04%. In Haiti, the prevalence was 36.5% of active cases of yaws among some 3.5 million people; this was reduced by mass campaigns to 0.57%.

ADULT SCURVY.

SINCE adult scurvy is now a relatively rare condition in English-speaking countries, a recent report of eleven cases by R. H. Culfort³ makes interesting reading. Ten of these patients were men, and most were elderly, retired men, living alone, subsisting on a diet of toast or bread and butter, with meat paste and tea. Three others were dyspeptics, keeping to a diet of milk, eggs, fish or chicken, and mashed potatoes. The last was a "vegetarian", whose diet consisted solely of wholemeal bread, margarine, cheese, milk, honey and eggs.

The clinical picture differed somewhat from that indicated by most text-book accounts of the disease. The fact that only one patient presented with the typical gum lesions of scurvy is partly accounted for by the fact that seven of the patients were edentulous. However, two of the remainder had apparently healthy gums. Spontaneous bruising was found to be the most characteristic symptom. All patients made a good recovery with doses of 600 to 700 milligrammes of ascorbic acid per day.

¹ *Circulation*, September, 1957.

² *New England J. Med.*, 1957, 257: 491 (September).

³ *Lancet*, 1958, 1: 454 (March 1).

Abstracts from Medical Literature.

MEDICINE.

Combined Treatment in Hypertension.

H. E. NUSSBAUM *et alii* (*Am. J. M. Sc.*, August, 1957) discuss an effective combination in the treatment of the hypertensive patient. As a result of studies with a host of therapeutic agents in more than 400 patients during the past four years, the authors are of opinion that mecamylamine offers certain advantages over other ganglion-blocking agents, and that the addition of meprobamate to the dosage regimen is highly desirable, especially in emotionally labile patients with moderate to severe hypertension. The major advantage of mecamylamine is that it is completely absorbed from the gastro-intestinal tract, and its duration of action is longer than other ganglion-blocking agents. Meprobamate is a helpful sedative and soporific for anxiety and tension without the recognized limitations of phenobarbital and reserpine. The threat of psychic disturbances, water retention, increased weight gain and persistent nasal stuffiness have caused the authors largely to abandon reserpine for meprobamate. The use of mecamylamine in combination with meprobamate was found highly effective. While this study showed that meprobamate, alone, had little, if any, hypotensive action, potentiation of the action of mecamylamine by meprobamate was evident in some patients. Also, subjective response was usually greater with the combination than with either drug alone. The present study was based on a series of 37 patients with moderate to severe hypertension treated as out-patients. The clinical notes of four illustrative cases are presented. Although it is impossible to predict how this form of treatment will modify the course of hypertensive heart disease, significant reductions in both systolic and diastolic blood pressures occurred in most patients. Also, changes in the optic fundi were often improved during the course of therapy, and there was marked relief of headaches and apprehension in almost every patient, if the dose was adjusted with sufficient care to suit individual needs. Inadequate adjustment of dosage leads to failure with most patients and loss of confidence in the therapeutic effects of the drugs. Side effects are difficult to avoid during hypotensive therapy, but the serious consequences resulting from them can be prevented. Of the 37 patients in this series, treated over a period of 17 months, the blood pressure of 28 was controlled successfully with mecamylamine. Meprobamate alone had no effect on the blood pressure of the same group. In combination, the two drugs provided objective and subjective improvement in 35 out of the 37 patients. Meprobamate facilitated management, adding to a sense of well-being, with loss of any chronic complaints of mild nature, and loss of apprehension in most patients. The initial dose of mecamylamine used was 2.5 milligrams;

taken three times a day after meals, but this dose was inadequate. The dose was gradually increased each week until an adequate reduction in blood pressure was elicited or side effects became troublesome. The majority of patients required at least 10 milligrams per day of mecamylamine, four patients required 60 milligrams per day, two required 75 milligrams per day, and one needed 90 milligrams per day, before satisfactory response was obtained. Initially, 400 milligrams of meprobamate was given twice a day, and later increased to 400 milligrams four times a day. No higher levels were needed. Constipation is the most common side effect, but this commonly coincided with a satisfactory reduction in blood pressure. Epigastric discomfort occurs sometimes, and is easily relieved by a slight reduction of mecamylamine dosage. Vertigo occasionally occurs, which is relieved by bed rest, or sitting down, or slight reduction of mecamylamine dosage. Headaches, which were a major complaint prior to treatment in 95% of the patients, persisted in only four during therapy.

and they were probably maintained on high fat diets since they were treated cases. It may be postulated that tuberculosis attacks a type of person not prone to heart attacks, but this can neither be proved nor disproved. Perhaps this antagonism can be explained by the hypothesis that tuberculosis infection provokes some response in the body which has a protective action against coronary thrombosis and thrombo-embolic phenomena in general. Thrombo-embolism and pulmonary infarction are said to be relatively rare in tuberculous patients. A circulating anticoagulant could explain these observations and, indeed, a circulating anticoagulant has been described in some tuberculous patients with abnormal bleeding tendencies. Further study of the relationship of tuberculosis to coronary thrombosis is indicated, for perhaps therein lies a clue to an effective prophylactic treatment against coronary thrombosis. Even now a safe tuberculous infection may be given in the form of B.C.G. vaccination.

Tuberculosis and Coronary Thrombosis.

J. H. ROGERS (*Ann. Int. Med.*, July, 1957) discusses tuberculosis and coronary thrombosis. Attention is drawn to the low incidence of coronary disease in various groups throughout the world. These groups include Orientals, some African tribes and American Indians, and possibly others. Attention has been also called to the low incidence of coronary disease which prevailed in countries of Western Europe during the war and immediate post-war period. In these countries prior to the war (as now), coronary disease had presented a serious problem. These observations have been largely responsible for the present popularity of the dietary or metabolic concept of coronary disease, since a substandard diet, low in fat, has been assumed to be a factor common to all. The purpose of this contribution is to add another group to the list of low coronary disease groups, to point out a possible relationship between this group and the others, and to make some speculations therefrom. It has been observed by many that the incidence of fatal coronary thrombosis in tuberculous patients is unusually low. A study of the death certificates of 325 patients afflicted with tuberculosis (ages ranging from 40 to 91 years) revealed that 18.8% died of coronary thrombosis. In a comparable non-tuberculous group, 29.2% died of coronary thrombosis. This difference is even more marked when only those between 40 and 60 years old are considered. The addition of the tuberculous group to the list of low coronary disease groups mentioned previously calls attention to the fact that these groups have something in common besides substandard diets, and that is a high incidence of tuberculosis. Also, in Western European countries during the war there was a marked increase in the incidence of tuberculosis. It would not appear logical to attempt to apply the dietary theory to the tuberculous group in the study, since they did not "waste away with consumption", but died of other causes;

Chlorpromazine Jaundice.

S. J. SKROMAK *et alii* (*Am. J. M. Sc.*, July, 1957) discuss their observations of chlorpromazine-induced jaundice with continued use of the drug. The clinical notes of two such cases are presented, wherein the drug was continued inadvertently without ill effect. The clinical picture of jaundice cleared and did not recur, despite continued therapy. This observation raises some question as to the necessity of discontinuing treatment because of the appearance of jaundice. The ability to continue chlorpromazine therapy despite the appearance of jaundice would be of some selective therapeutic value, especially in neuro-psychiatric patients. The symptom complex of chlorpromazine-induced jaundice is similar to that of extra-hepatic jaundice. The icterus may be preceded by anorexia, nausea, and perhaps vomiting. The jaundice may appear as early as nine days or as late as five weeks after institution of drug therapy. The duration of icterus has been reported to vary from 48 hours to three months, and the drug dosage is not related to the appearance of jaundice. The liver may enlarge, but is usually not tender, although it may be tender in some cases. A mild eosinophilia may be present and there is an elevation of both serum bilirubin and cholesterol levels. The serum alkaline phosphatase is elevated and may remain so after the jaundice has cleared. The cephalin flocculation test is usually negative, but may be positive. The pathogenesis of the condition is still obscure, but current thought revolves around several possible mechanisms. One is that of hypersensitivity to the drug. The other postulates the removal of some essential metabolite from the liver as a result of the drug action. The theory most acceptable to the authors is that injury or functional disturbance of the hepatic cells or cholangioles results in alteration of normal bile hydration, thus increasing the viscosity of bile. The pathology of chlorpromazine-induced jaundice is similar to that of extrahepatic obstructive jaundice, and is referred to as primary intrahepatic cholestasis. Cortisone is known to have two effects on bile. One

is hydrocholeresis or an increase in bile volume, and the other is choleresis or an increase in concentration of bilirubin and bile salts in the bile. A recent report cites the disappearance of chlorpromazine-induced jaundice after two days of cortisone therapy. It is interesting to speculate on the possibility of a temporary interference with, or relative insufficiency of, cortisone activity, in the hepatic cells or bile canaliculi, in those patients who develop jaundice on chlorpromazine therapy. It is suggested that under strict control in hospital such jaundiced patients might be cautiously continued on this therapy, since additional evidence is necessary to confirm these observations before recommending this practice.

Antibiotic Combinations.

W. F. JONES, JUNIOR, AND M. FINLAND (*New England J. Med.*, September 12 and 19, 1957) report comparisons of the in-vitro activity, and the antibacterial action of blood after oral administration of each of the following: tetracycline, erythromycin, oleandomycin, spiramycin and combinations of tetracycline with each of the other three antibiotics. They were tested against Gram-positive cocci. Erythromycin alone was superior to oleandomycin or spiramycin in its activity against all strains that were sensitive to erythromycin. In those resistant to erythromycin, there was considerable variation in susceptibility to individual agents, but no combination was superior to the more active component alone, and no combination was better than either tetracycline or erythromycin alone. Even in a strain more sensitive to oleandomycin alone than to erythromycin alone, the effect of tetracycline and erythromycin together proved better than tetracycline and oleandomycin together. It is concluded that oleandomycin and spiramycin are sufficiently inferior in Gram-positive coccal infections to indicate that their adoption for general use is unwarranted. They should be reserved for use alone, only when the infection has been shown to be resistant to erythromycin and tetracycline. The use of combined antibiotics involving spiramycin or oleandomycin as one part of the combination represents bad practice. No combination including combinations with tetracycline showed synergism.

“Chlorothiazide”: An Oral Diuretic.

G. E. SCHREINER AND H. A. BLOOMER (*New England J. Med.*, November 21, 1957) report on the effects of “Chlorothiazide”, an oral non-mercurial diuretic acting independently on the renal tubular reabsorption of sodium and chloride, on 36 patients with cardiac, hepatic or renal oedema. The dosage was five to 10 milligrammes per kilogram of estimated body weight every six hours. Five of six patients with congestive cardiac failure responded with satisfactory diuresis, one patient having previously been unresponsive to other forms of diuretic therapy. In the nephrotic syndrome five out of nine courses in seven patients gave favourable responses with significant loss of body sodium and water. In four cases of cirrhosis with ascites satisfactory responses occurred, although in three cases there had been resistance to

mercurial diuretics. In some cases there was an increase in the urinary output of potassium and chloride without loss of sodium. No serious side effects were observed. In chronic renal insufficiency with azotemia, “Chlorothiazide” failed to produce adequate diuresis because of marked reduction in the glomerular filtration rate. It is concluded that “Chlorothiazide” represents a significant advance in diuretic therapy and is capable of overcoming the salt retention caused by adrenal steroids.

Myocardial Infarction and Heart Size.

M. M. WEISS AND M. M. WEISS, JUNIOR (*Am. J. M. Sc.*, August, 1957) discuss the effect of myocardial infarction on the size of the heart. A report is based on a follow-up study of 489 patients who survived an acute myocardial infarction for at least two months, and who had a normal sized heart at the time of the infarction. Only those patients who had recovered from their presumed first infarction were included in the study. The majority of the patients were observed for one to 10 years. Only 2% (eight cases) developed cardiac hypertrophy in the absence of generally accepted factors such as hypertension, valvular heart disease or *cor pulmonale*. The case reports of these eight patients are summarized. Cardiac enlargement was first noted from six months to 13 years after the first infarction. All of the eight patients who developed cardiac hypertrophy had associated congestive heart failure. Multiple myocardial infarctions did not cause cardiac hypertrophy in the absence of congestive failure. The opinion is expressed that cardiac hypertrophy develops with congestive failure, which in turn results from the development of a myocardial aneurysm or extensive myocardial fibrosis, or both, as complications of the myocardial infarction.

Steroid Therapy in Mumps Orchitis.

G. N. ZELUFF AND T. J. FATHORREE (*Ann. Int. Med.*, May, 1957) discuss the use of steroid therapy in mumps orchitis and present the history of four cases so treated. Mumps is an acute infectious disease of viral origin affecting primarily the parotid glands, but often involving the testicles, ovaries, central nervous system and pancreas. The complication of orchitis seems confined almost entirely to adults, and usually appears as the parotitis is subsiding, somewhere between the fifth and seventh days. It may be unilateral or bilateral and not infrequently is preceded by an epididymitis. The incidence is generally said to be of the order of 20% of all cases of adult mumps. An appreciable amount of atrophy of the testis occurs in at least half of these patients, but there is a real difference of opinion as to the significance of this fact as a cause of sterility. Treatment has varied in the last few decades, but has been consistent in its relative lack of success. The authors used hydrocortisone or prednisone or ACTH with dramatic response in the four cases cited. The effectiveness of antibiotics has been uniformly disappointing in mumps orchitis. If therapy is instituted

sufficiently early with the corticoids, it is probable that there will be no residual damage to the testes, apart from the fact that the severity of this painful and disabling condition is greatly reduced. It is suggested that all cases of mumps orchitis be treated promptly with steroids except in the presence of the usual unrelated contraindications to this form of therapy.

Megaloblastic Anemia After Partial Gastrectomy.

L. D. MACLEAN (*New England J. Med.*, August 8, 1957) from Minneapolis investigated the vitamin B_{12} absorption of 13 patients who had previously undergone partial gastrectomy. One who had undergone a segmental resection for a gastric ulcer failed to absorb vitamin B_{12} . Examination of the resected stomach in this case revealed extensive atrophy of the mucosa. A follow-up of 1550 patients who had previously undergone partial gastrectomy showed nine who had megaloblastic anemia, commencing from two to 12 years afterwards. Review of the resected stomachs from these patients revealed similar histological changes. Three initially had benign gastric ulcers (two with associated duodenal ulcer) and all had free acid in the gastric juice before surgery. All operations in those who developed megaloblastic anemia had been of the Pólya type, and the anemia had responded to liver or vitamin B_{12} , without folic acid supplement.

Prednisone in Congestive Heart Failure.

L. B. GUTNER *et alii* (*Am. J. M. Sc.*, September, 1957) discuss the use of prednisone in congestive heart failure and base their remarks upon a study of 11 patients. These patients, who were suffering with congestive cardiac failure necessitating maintenance digitalis therapy, were given prednisone orally in doses of 20 or 40 milligrammes per day. The urinary excretions of sodium, potassium and 17-ketosteroids were observed before and after corticoid administration. The overall effects were increased sodium and potassium excretion, decreased output of 17-ketosteroids, no essential change in weight or blood pressure, and an amelioration of the cardiac status. Prednisone may therefore safely be administered to patients in congestive cardiac failure. The possible mechanisms of the action of prednisone in congestive heart failure are discussed.

Smoking and Diseases.

R. G. BROWN, T. McKEOWN AND A. S. W. WHITFIELD (*Brit. J. Social Med.*, July, 1957) report an investigation upon men in the seventh decade of life in Birmingham, England, comparing the incidence of diseases in those who had smoked heavily and those who had not smoked at all. Although there was no difference in the incidence of bronchitis according to social class among non-smokers, there was a much higher incidence of bronchitis in those who had been heavy smokers, and the difference was greater in the lower social groups. Peptic ulcer also showed a higher incidence in smokers, but smokers fared no worse than non-smokers with regard to the incidence of coronary artery disease, hypertension and hernia.

British Medical Association.

NEW SOUTH WALES BRANCH NEWS.

The following three letters are published at the request of the Assistant Medical Secretary of the New South Wales Branch of the British Medical Association. The first of these, dated February 21, 1958, was forwarded to all Members of the Legislative Council and of the Legislative Assembly in N.S.W. The second letter, dated March 4, 1958, was forwarded to the Honourable W. F. Sheahan, N.S.W. Minister for Health. Both of these letters were sent from the N.S.W. Branch of the B.M.A. The third letter is the reply received from Mr. Sheahan.

[COPY.]

Medical Education.

Dear Sir,

You have undoubtedly read in the Press within this last week or two that the New South Wales Branch of the British Medical Association has decided to appoint a Committee to consider medical education. The term "medical education" is used here in the broadest sense, for it is intended to cover undergraduate, graduate and post-graduate education.

Naturally, you are probably wondering why it is necessary for the British Medical Association to appoint such a Committee when the Government has already appointed a Committee for this purpose.

Briefly, there are two main reasons:

1. The magnitude of the problem and the consequent need for it to be considered from every angle.
2. The desire of the British Medical Association to submit to the Government its considered views on this important matter.

Medical education covers a vast field, and it is of the utmost importance that it be fully realised by everybody interested in the matter that any investigation of it cannot be carried out in a short period. This can be well illustrated by reference to the work of a number of committees appointed in other parts of the world at various times.

In 1910, there was published the report of the Carnegie Foundation for the Advancement of Teaching on Medical Education in the United States and Canada, which was prepared by Abraham Flexner. It took five years to complete.

In 1925, the Commission on Medical Education was organised by the Association of American Medical Colleges for the purpose of making a study of the educational principles involved in medical education. The Director of Study was Willard C. Rapleye, A.M., M.D. The final report of the Commission was published in 1932.

In 1944, the Ministry for Health, Great Britain, published the report of the Inter-Departmental Committee on Medical Schools. Under the chairmanship of Sir William Goodenough, the report took two years to prepare.

In 1945, the Medical Curriculum Committee of the British Medical Association in Great Britain was appointed by the Council of that body to review the Association's report on Medical Education in the light of later developments and the requirements of medical practice. Its chairman was Professor Henry Cohen (now Lord Cohen). The Committee's report, "The Training of the Doctor", was published in 1948.

The lengthy periods which each of the above-mentioned committees took to produce their reports indicates the magnitude of the problem and stresses the need for it to receive the greatest consideration.

It is a matter which in the public interest cannot be hurried. It involves more than the consideration of whether another University is necessary and where it should be established, or whether there should be a number of pre-clinical schools and of other matters to which the Murray Report refers. It may be said of the Murray Report that it but touches the very fringe of the subject.

With regard to the intention of the British Medical Association to produce a report, there is a sincere desire on its part to submit to the Government its views on this matter.

The Association is a body which may well be regarded as representing the medical profession. Its members are actively engaged in the teaching of students during their University career; in the training of graduates as Resident Medical Officers in hospitals and in subsequent post-graduate

training. It is therefore a body competent to investigate this matter, and it has taken steps to ensure the competency of its Committee by issuing invitations to representative bodies, interested in medical education, to appoint representatives to the Committee.

What the British Medical Association desires to stress is that there should be no undue haste in this matter. It is fully realised that all necessary steps must be taken to meet the requirements of the future. The British Medical Association is very jealous of the standard of medical practice in this country. It desires that that standard be maintained and that no precipitate action be taken which might lower it.

The Association hopes to make its report within a reasonable period of time. It will issue from time to time interim reports, but the full final report may take some time.

The Association trusts that the authorities concerned with the establishment of a new medical school and with medical education in general will hasten slowly and give the matter the full consideration it deserves.

Faithfully yours,

(Signed) J. G. HUNTER,
Medical Secretary.

February 21, 1958.

[COPY.]

The Honourable W. F. Sheahan, Q.C., LL.B., M.L.A.,
Minister for Health,
52 Bridge Street,
Sydney, New South Wales.

Dear Sir,

In the issue of the "Daily Telegraph" of the 27th February, 1958, you were reported as having stated in Parliament that those persons with ideas on a second medical school should submit them by 13th March.

As indicated in the letter addressed to you and Members of the Legislative Council and the Legislative Assembly by the Medical Secretary on the 21st February, the Association is sincerely desirous of submitting its views on all aspects of medical education to your Government.

There is no doubt in the minds of the majority of people that the intended actions of the Government in relation to the establishment of another medical school arise from the Murray Report.

The Murray Report states:

"There appears to be every justification for the establishment of a second medical school in New South Wales, where already the University of Sydney is attempting to cope with far greater numbers than the University of Melbourne. The present policy of admitting great numbers of students to the Sydney school when it is possible to accommodate perhaps only 50 per cent. of these in the clinical years is open to serious question; it places an unjustifiable burden on the Faculty of Science and the pre-clinical departments, while leading inevitably to the disappointed hopes of students who, in this instance, it appears, must fail. If there should be a new medical school, there is much to be said for placing this in the N.S.W. University of Technology."

It cannot be said that the Committee on Australian Universities under the chairmanship of Sir Keith Murray has made a firm recommendation as to where a new medical school should be established. It would appear, therefore, that it is a matter which requires a good deal of consideration.

The Committee on Australian Universities had a vast field to cover in a short time. It dealt with all faculties and not only the Faculty of Medicine, and its report did not deal in detail with medical education. That there would be difficulties in covering a vast field was appreciated by the Prime Minister when he wrote to Sir Keith Murray, stating: "I recognise that in the space of three months, the Committee will of necessity be forced to limit its enquiries and deliberations to a relatively small number of topics." In presenting its report the Committee wrote as follows:

"We have outlined what we consider to be the most serious problems in the situation as we see it today; they will become even more urgent in the immediate future, faced as the universities are with an increase of over 100 per cent. in their potential enrolments over the next ten years. The time at our disposal has been too short adequately to study all the issues confronting them, but we have concentrated our attention on what we consider the most important, and we have made recommendations on what we think should be done immediately to meet a critical situation."

Having regard to all the circumstances, it is considered that every aspect in connection with medical education should be thoroughly examined. If particular reference is made in this letter to the proposed new medical school, it is not desired to stress this particular matter, nor to submit any sectional views on it. It is but one facet of a large problem. However, the Committee that has been appointed by the Association to consider medical education would greatly appreciate the opportunity of examining any proposals in connection with the establishment of a new medical school. It feels, however, that it could not do this thoroughly by the 13th March, and that any advice which it might be able to give by that date would be of an ill-informed nature.

It is asked, therefore, that you extend this date to a much later date and allow all aspects of medical education to receive the full consideration due to it.

Faithfully yours,

(Signed) HUGH HUNTER,
Assistant Medical Secretary.

March 4, 1958.

Minister for Health, New South Wales.

11th March, 1958.

Dr. H. Hunter,
Assistant Medical Secretary,
British Medical Association,
135 Macquarie Street,
Sydney.

Dear Dr. Hunter,

I desire to acknowledge your letter of 4th March, 1958, concerning an article which appeared in the *Daily Telegraph* of 27th February, 1958, in which it was reported that I had stated in Parliament that those persons with ideas on the second medical school, should submit them by 13th March. I note that your Association is desirous that this date should be extended to a much later date.

You will be further advised in this matter.

Yours faithfully,

W. SHEEHAN,
Minister for Health.

Dut of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE MEDICAL ADVISER TO THE NEW SOUTH WALES GOVERNMENT.

[From the *Australasian Medical Gazette*, January, 1893.]

As a consequence of ill health and to the universal regret of the profession, Dr. Norton Manning has felt it necessary to resign the appointment which he has held as medical adviser to the New South Wales Government and President of the Board of Health of that Colony. He will, however, retain that of Inspector-General of the Insane.

Our expressed fear on his accepting the offices which he has now resigned, that the combined duties would prove more wearing than his strength would bear, has unfortunately proved a correct preision, and it is exceedingly fortunate that the colony can still avail itself of his services, which could not be adequately replaced in the supervision of the institutions for the treatment of its insane. It should not be forgotten that Dr. Manning did not seek his late offices, but allowed himself to be appointed from a sense of public duty, for it is an open secret that by doing so he perhaps prevented circumstances arising which might have proved a serious peril to the safety of the public health and well-being. He is succeeded by Dr. Anderson Stuart, Dean of the Faculty of Medicine and Professor of Physiology at the Sydney University. This gentleman is well fitted for the position to which he now succeeds, being thoroughly capable with much force of character. His capabilities as an administrator have been thoroughly proved by the efficiency of the School of Medicine of which he is the head, which is due to his power of organization.

Correspondence.

EPISIOTOMY.

SIR: Congratulations to Dr. L. J. Shortland on his provocative letter regarding episiotomy (M. J. AUSTRALIA, February 22, 1958, page 266) and his excellent record in preserving the intact perineum. Presumably Dr. Shortland is referring to normal uncomplicated deliveries, and in general most practitioners interested in obstetrics will agree. The generally accepted reasons for episiotomy are:

1. An incision of access.
2. The debatable "prophylactic episiotomy", with or without forceps extraction to prevent genital prolapse.

It is in regard to this second reason that most of the contentious argument is centred. Indeed, the great British obstetrician, Chassar Moir,¹ in speaking of prophylactic episiotomy, was moved to ask the pertinent question "If prophylactic, prophylactic against what?". He points out that the operation is abused by being employed for trivial reasons, and by operators who care little for the finer points of obstetric art.

The proponents of "prophylactic episiotomy" state that an overstretched and devitalized perineum (the common meeting place for insertion of the muscles of the pelvic floor) causes a loss of functional capacity, so that often, even after a latent period of many years and sometimes coinciding with menopausal atrophy, the supports of the uterus and bladder neck yield, giving rise to prolapse and stress incontinence.

No one would deny that if the perineum is kept on the stretch for a long time by the baby's head, then pressure and shearing strains are transmitted to the back of the pubic symphysis and region of the bladder neck, so that its supports—the anterior fibres of the pubo-rectalis and pubo-vaginalis—may become torn across or permanently weakened. It is a poor obstetrician who would not rescue the parturient in the face of a prolonged second stage. The rescue is usually effected by a forceps delivery with episiotomy, which, however, in this instance is an "incision of access" for an abnormal development in labour.

Routine episiotomy in *primigravidae* is a product of American obstetrics, its routine use being advised by De Lee² in anticipation of fetal or maternal distress, an idea supported by Professor Eastman and Professor Te Linde,³ who state that it will largely prevent prolapse and stress incontinence. On the other hand, Moir (page 46) states that episiotomy is seldom necessary in normal deliveries, and the chief objection is that every delivery is thereby converted into an operative procedure. A more blunt and emphatic point of view is advanced by Malpas:⁴ "In its extreme forms episiotomy is indicative of a common frame of mind, obtaining not only in obstetrics but other branches of medicine, that the competency of the normal mechanisms of the body is to be distrusted. An episiotomy should be done for immediate obstetrical indications alone, and not to prevent a prolapse later." Equally emphatic is Donald,⁵ who states that to withhold episiotomy when indicated would be wanton; nevertheless, it constitutes a mutilation, and if ruthlessly abused without good reason it will leave a number of women exposed to the likelihood of further perineal troubles on subsequent deliveries and occasionally an unsatisfactory scar and dyspareunia. Furthermore, as an alternative injury to a second degree tear, Donald regards the value of episiotomy as debatable, "and to inflict a cut for no other reason than to prevent a tear is of dubious advantage because an episiotomy may be more extensive than actually necessary".

Apart from the question of episiotomy in the prevention of remote genital prolapse, it would seem that the ability of the perineum to stretch without tearing depends on:

1. The degree of flexion of the head in normal vertex presentations. If the head is allowed to extend too soon against the soft tissue resistance of the perineum, instead of the smallest diameter of the fetal head (the sub-occipito-

¹ "Munro Kerr's Operative Obstetrics", Sixth Edition, 1956, Baillière, Tindall and Cox, London, page 907.

² *Am. J. Obst. & Gynec.*, 1920, 1: 34.

³ Quoted in "British Obstetrical and Gynaecological Practice", 1955, William Heinemann, London, page 789.

⁴ "Genital Prolapse and Allied Conditions", 1955, Harvey and Blythe, London, page 33.

⁵ "Practical Obstetric Problems", 1955, Lloyd-Luke (Medical Books), London, page 403.

bregmatic diameter of 9.5 centimetres) being accommodated by the vulval outlet, the sub-occipito-frontal diameter of 10 centimetres impinges suddenly on the perineum. The gradual encroachment on the fourchette of this half-centimetre difference is, in my opinion, the most crucial and exacting part of a normal delivery in the avoidance of laceration.

2. The speed at which delivery is effected. This implies delivery of the head between pains, for then it is most easily controlled. If Ritgen's manoeuvre is carefully and slowly performed on the crowned head between contractions with downward pressure on the occiput to maintain complete flexion until it is born almost as far as the bridge of the nose, supplemented by such manoeuvres as "guarding the perineum", then the head is born with the smallest diameter always presenting.

3. The degree of muscular relaxation afforded by anaesthesia, as pointed out by Dr. Shortland in his letter. Of the general anaesthetics, in my opinion by far the most efficient in this respect is chloroform (well administered and mindful of its dangers), although personally I favour pudendal block for all deliveries.

4. The avoidance of any sudden stress such as occurs if the patient coughs or vomits when a general anaesthetic is used.

5. The "elastic index" of the connective tissues. It is said that when the *striae gravidae* are absent, or fine and narrow, the elastic index is high, and the connective tissues will stretch, a tear being unlikely. When they are broad and coarse the index is low.

6. The care with which the posterior shoulder is delivered. The tension in the perineum is increased in the following conditions:

1. If the pubic arch is narrow, with consequent posterior displacement of the head.

2. If scar tissue is present from previous obstetric trauma or repair operation.

3. If the presentation is abnormal: e.g., a face-to-pubes, or a breech delivery.

4. If there is need for intrauterine manipulations: e.g., manual or instrumental rotation of an unrotated head.

An incision of access is desirable in connexion with these four conditions, as well as in cases of premature labour and fetal distress. In all other cases careful attention to minutiae in delivery will avoid both episiotomy and laceration.

Finally, from the humble and earthy point of view of the busy general practitioner doing obstetrics, the preservation of the perineum has two classical and uncontroversial advantages:

1. During daylight hours, office appointments are not upset by time-consuming episiotomy or laceration repairs.

2. At night it favours more sleep.

Yours, etc.,

ALAN R. HOYLE.

17 Urabatta Street,
Inverell,
New South Wales.
February 25, 1958.

SIR: Dr. L. J. Shortland's letter on "Episiotomy" (M. J. AUSTRALIA, February 22, 1958) was refreshingly frank, but one might be excused for asking if a publisher's error was responsible for its appearance in "Correspondence" instead of in its proper place in "Out of the Past".

Yours, etc.,

A. M. HILL.

111 Collins Street,
Melbourne,
February 28, 1958.

HOSPITAL TEACHING.

SIR: In his interesting address (M. J. AUSTRALIA, March 1, 1958, page 279) Professor Neville G. Sutton quotes the conclusions of a meeting of the professors of clinical departments of the Australian medical schools on certain aspects of teaching. The fourth conclusion, "The payment for such teaching is at present purely a nominal amount, and since it is clear that the teaching effort will continually increase, an adequate and realistic salary will have to be paid by the universities. The teaching duties should be clearly dis-

tinguished from duties of caring for the patients", requires some comment.

The idea of distinguishing "treatment" from "teaching" duties in clinical teaching is completely artificial and bad, because (a) the patient is both subject for teaching and object of treatment, often within the same five minutes, (b) the visiting staff member performs both "teaching" and "treating" functions simultaneously, (c) the benefits of good teaching are shared by the patient, the teacher, the student and the whole community. The patient benefits from better treatment, as was recently demonstrated numerically by Lee, Morrison and Morris (*Lancet*, October 19, 1957, page 785), the teacher benefits by higher professional standards, the student by learning his profession, and the community by better treatment of its members in hospital, by higher standards of the consultants available to it, and by the better training afforded to medical graduates and undergraduates in general.

The difficulties and fallacies inherent in the idea of distinguishing teaching duties from duties of caring for patients are obvious. The suggestion can only have been made as a somewhat short-sighted attempt to solve the purely administrative problem of who is to pay.

It is submitted that the implementation of such a suggestion would be destructive in that it would engender in hospital and university administrative staffs, in government departments, and ultimately in the community as a whole, the impression that treatment and teaching are separate, the former for the benefit of the patient, and the latter for the benefit of the student.

A more constructive approach would be to accept and actively promulgate the fact that there can be no separation of the duties of the clinical teacher; and further, that as the community derives such benefit from teaching in hospitals, it should be prepared to meet part of the teaching bill, and not leave all the cost to be met by the universities.

In the event of such an approach being adopted, the paid visiting staff of a teaching hospital would be appointed according to the teaching treatment requirements of the hospital, and paid entirely by the hospital. The hospital in turn would receive partial payment from the university. Such a principle would pave the way for a constructive development of clinical teaching and avoid a most undesirable dichotomy.

Yours, etc.,

Ballow Chambers,
Wickham Terrace,
Brisbane.

March 6, 1958.

D. A. HENDERSON, M.R.C.P.

Obituary.

SIR THOMAS DUNHILL.

We are indebted to Sir Hugh Devine for the following appreciation of the late Sir Thomas Dunhill.

Sir Thomas Dunhill, G.C.V.O., C.M.G., M.D., F.R.C.S., F.R.A.C.S., extra surgeon to the Queen, and consulting surgeon to St. Bartholomew's Hospital, was a great Australian who became a legend in his lifetime. His distinctions were international, and his contributions to the advancement of medical science were so wide that it is immaterial whether he finally wore the crown of his success in England or Australia. His pioneer work in the field of thyroid surgery, for example, has no frontiers. He died at Hampstead on December 22 last year at the age of 81. It would be wrong to suggest that Tom Dunhill had to go abroad to win fame and recognition. He did brilliant things in Australia, and has left enduring achievements behind him. As one of his colleagues at the beginning, and a lifelong friend, I believe the story of his work here is essential to the balance of any biographical note.

Thomas Peel Dunhill was a country boy, the son of John Webster Dunhill, and was born at Tragowel, Victoria, on December 3, 1876. When he left school he worked as an assistant in a chemist's shop to earn money for his medical education, and that experience proved invaluable to him. It filled his practical mind with a common sense that never failed him. He won an Exhibition to the University of Melbourne, took first-class honours in most examinations, and won the Beanean surgical scholarship. He graduated in

1903, and took his M.D. in 1906. His target was a surgeon's post at the Melbourne Hospital, the one established teaching hospital of that day, but the latter-day University Electoral Boards did not then exist, and unless a young doctor was specially favoured by friends and finance, his chances of getting there on his merits were limited. Dunhill became a tutor at Ormond College, where he made a wide circle of literary friends and steeped himself in the surgical teaching facilities of the hospitals and the University. This is where he began his now-famous research into the thyroid gland and the cause of Graves's disease. He practised the operation of thyroidectomy on goats—which he milked himself, then distributing the milk to patients. His ancillary researches were carried out in the laboratories of his professorial friends, who freely gave him the use of the facilities he needed. In 1908 he joined the staff of the new St. Vincent's Hospital, which became a University Clinical School in 1909. He had the vision to see great things

medical teaching was suffering, and there was a pressing demand for more teaching hospitals. Dunhill was in the van of the reforms, and a standard-bearer for progress. He was impatient with inefficiency and never concealed it—a trait he carried with him throughout his life. He was forthright in his work, poised and calm in a crisis. That was the surgeon. The man was a warm and sensitive personality loyal in his friendships, quiet and courteous in manner, and forever seeking to cross new horizons.

A personal tragedy, when he was on the threshold of his career, gave to his later work a missionary zeal. His brother John, with whom I had shared rooms in college and who was a doctor of exceptional brilliance, died in Melbourne in tragic circumstances, striving to save a desperately ill septic patient. This had a profound effect on Tom. They had been inseparable, and, in an effort to fill the vacuum, he threw himself into work with a restless, feverish energy, which finally led to rich achievements and, though unsought, to high personal distinctions.

It is impossible, within reasonable space, to record all the shining milestones in his distinguished career. A selection only can be made. His first paper on the treatment of goitre by partial thyroidectomy under local anaesthesia was published in the *Inter-Colonial Medical Journal of Australasia* in 1907. At that time the resection of one lobe of the thyroid, together with the ligation of the main artery of the opposite side, was the surgeon's limit. Dunhill decided to venture further by resecting half of the second lobe in the more severe cases of Graves's disease. It was a decision courageously taken, after long and anxious consideration. It was highly successful, and his methods became the pattern for surgeons all over the world. In 1912 Dunhill visited the United States and Britain, and while in London, described the treatment of simple goitre to the section of surgery of the Royal Society. During World War I he served with the Australian Imperial Force, mostly in France, and rose to the rank of colonel. His brilliant work as a military surgeon attracted attention, and in 1918 he became consulting surgeon to the British Army in France. He was mentioned in dispatches three times, and was created C.M.G. in 1919. In that year he published a paper in *The British Journal of Surgery* on the surgical treatment of exophthalmic goitre. He had made his mark then in two hemispheres, before returning to Australia.

Within two years he was outward bound again for London, turning his back on the rich personal rewards that were his for the taking in private practice in Australia. He went at the invitation of the late Professor George Gask to be first assistant in the first professorial surgical unit which Gask was forming at St. Bartholomew's Hospital. Gask knew his man; he had watched his work during the war, and being eager to develop surgery of the chest, he picked Dunhill as the best man for the job. It was not often in those days that London came to the Antipodes for the best. Dunhill quickly made his mark, not only at St. Bartholomew's but on British surgery. He became, after Sir James Berry, the pioneer of thyroid surgery in Great Britain. He was leading, and a legion of younger men began to follow. He summed up his work in the Lettsomian lectures before the Medical Society in London in 1937. In 1941 the same society awarded him the Fothergillian gold medal. He was a full surgeon at St. Bartholomew's, and was appointed consulting surgeon on his retirement in 1935. At this stage he published a description of his operation for the removal of intrathoracic tumours by the transsternal route, and placed on record one more significant advance in thoracic surgery. At the Royal College of Surgeons he gave the Arris and Gale lectures on carcinoma of the thyroid in 1931, and on diaphragmatic hernia in 1934. His work on diaphragmatic hernia, and on pharyngeal diverticulum, was outstanding, and has become part of the education of young surgeons. It should not be obscured by his recognized pre-eminence in thyroid surgery. In 1939 he achieved the distinction of election to an honorary fellowship of the Royal College of Surgeons of England, an accolade usually reserved for foreign surgeons. The College awarded him the Cecil Joll prize in 1950, and in the following year he delivered the Joll memorial lecture on thyrotoxicosis. Sir Thomas Dunhill was a member of the British Medical Association for 50 years, and served on the Central Council from 1921 to 1936. He was also a member of the Dominions and other committees of the Association. He never severed his Australian loyalties, and in 1930 was elected a Fellow of the Royal Australasian College of Surgeons. He "came home" on a visit in 1935, and presided at the Section of Surgery at the annual meeting of the British Medical Association in Melbourne. During this visit, he was given the honorary degree of M.D. by the University of Adelaide. In World



ahead. With the prospect of the development of this hospital as a clinical school and a teaching hospital, we shared our dreams in those days as well as our work. They were exciting days, full of change and growth, and doors were opening on broad vistas in the surgery of medical science. I was Dunhill's assistant. His mind reflected an ideal spirit of medicine. Six months before he died, he wrote to me from London. It was a nostalgic letter, written from the summit, about those days when we worked together in the lowlands.

Those were great days. I remember spending most of my time during the first year or two on a continuous triangular circuit—Professor Allen at the University, Mother Berchmans at St. Vincent's, and the Chief Medical Officer of the City Council (Colonel Norris), who finally gave what he called his "permissive tolerance" for the use of the semi-basement at St. Vincent's for a teaching hospital.

What fun it all was, and how brilliantly St. Vincent's has kept the running so high ever since. Furthermore, we woke up the authorities to the knowledge that they could no longer keep ill-qualified surgeons on the staffs of the big hospitals.

During that period, reform had to go hand in hand with progress. The big hospitals were becoming out of date,

War II he was consulting surgeon to the second Australian Imperial Force, with the rank of brigadier.

His association with the Royal household extended over a period of thirty years. He was appointed surgeon to the Royal household in 1928, and honorary surgeon to King George V in 1930, to Edward VIII in 1937 and to George VI. In 1939 he was appointed sergeant surgeon to the King, and in 1952 extra surgeon to the present Queen. His honours multiplied. He was created K.C.V.O. in 1933, and promoted G.C.V.O. in 1949, after King George VI had an operation for lumbar sympathectomy. He also attended the King in 1951, when a lung resection was performed.

Sir Thomas Dunhill's wife, Mrs. Edith Florence McKellar, died in 1942. There were no children of the marriage.

This is not the moment to make a final evaluation of Tom Dunhill's work. What he did will last; it has been passed on, and medical science and the practice of surgery are richer for the fruits of his intellect and his practised hands. He truly walked with kings.

SIR HUGH POATH writes: It seems reasonable to claim the late Sir Thomas Dunhill as one of our most distinguished Australian surgeons, even though the greater part of his professional life was spent in London. One cannot call to mind another Australia surgeon who, after achieving a leading position in one of our great cities, had the pluck to venture into the home of British surgery, and by sheer merit, courage and determination achieve a dominant position among the leaders of this branch of medicine, and in due course receive selection as a surgeon to the Royal family.

To those who were privileged to know him, his success overseas was not altogether surprising; apart from his specialized knowledge in surgery, he had an innate courtesy, a charm of manner and a gift of making lasting friendships that is accorded to very few. He was known affectionately to all his friends as "Tommy", and inevitably could be relied upon to share his wonderful store of knowledge with any who cared to approach him, being particularly interested in the younger men. He seemed always frail and at times almost ethereal, making one wonder if he had the stamina to stand up to the rigorous demands of high-grade surgery, but as he lived to the age of 81 years, he must have been moulded in similar form to the finest steel—and of the stainless variety as well. To him belongs the credit for placing the technique of surgery of thyrotoxicosis upon a solid foundation, which, although expanded over the years, has remained the basis of modern practice.

He was drawn to simple pleasures, and in a recent notice Alec Chisholm refers to his interest in Australian bird life, and mentions that, on seeing a film of Australian wild life, "although appreciative of the studies shown, he [Sir Thomas] was even more interested in the faces of the audience, who, looking at pictures of the lyrebird and bower-birds, seemed to find difficulty in believing the evidence of their eyes".

In his last letter to the writer from North End Avenue, London, dated July 12, 1955, he commented that "for the first time I am living on soil on which azaleas and rhododendrons thrive. I am getting some of the pleasure from them that you get from your orchids, but thank God no more consultations and operations".

So "Tommy" has gone to his long rest, having helped to make the world a little better for his sojourn and leaving pleasant memories among his friends.

PROFESSOR HAROLD DAW writes: Tommy was one of the original fishermen on the Snowy with Harry Stephens, Richard Stawell, John Latham, Barnet Allen and others and fished for some years before 1918. He was also an enthusiastic canoeist and had done nice exciting trips over various rivers. He joined our club after the first World War in the middle twenties, and though he often said that he would come out and fish, he never did so, though he paid his fees. He became an honorary member a few years ago when he was 70. In England, of course, he was a very active fisherman; he had a place at Pangbourne and fished the Test regularly, and was a member at Eden Hall on the Eden in Cumberland, where I fished with him in 1930. He later became more enthusiastic about salmon on the Chartres; he did some salmon fishing in England and Scotland, where he had plenty of friends, but his real love was the west coast of Norway. Here for many years he and his friends as a syndicate had beats on various rivers, at first on the Laerdal river at the top of the Sogne Fjord, where I fished with him in 1939 and where I saw him land a 45-pounder, the best for that season. Later he went

further north, to a place just south of Narvik, where the estuary was bigger, and there he mainly fished from a boat, as the wading was a bit tough and he was not so strong. He retained to the end his extensive enthusiasm for all things pertaining to his fishing, and must have fished in a great number of places in Scotland and Ireland, both for trout and salmon.

MR. RUPERT SCOTT, F.R.C.S., has supplied the following copy of the remarks made by SIR JAMES PATERSON ROSS at Sir Thomas Dunhill's funeral.

We who knew and admired and loved Sir Thomas are met together to honour his memory, not in a spirit of mournfulness, for that would not please him, but in a spirit of thankfulness, to offer praise to Almighty God, and to express as best we may our thankfulness to Him for one who lived a life devoted to the service of his fellow men and women, yet a life which had in it so much besides professional work.

It is a heavy responsibility to speak to you, and if possible for you, because our hearts are full, and then silent thought may be more satisfying than speech. Yet I am accepting the responsibility for two reasons: first because I was privileged to know Sir Thomas almost as a son, and secondly because less than a year ago I had the opportunity of meeting many of his friends in Australia and of finding out more completely than before what he had meant to them.

In Brisbane I met a gentle, humble, yet most distinguished retired canon who had helped Tom to learn enough Latin to enter the University of Melbourne, and as I talked with him I realized that they loved each other as brothers.

In Melbourne I met medical men who were his friends from their student days: the theatre sister, now an old lady, who helped him with his first thyroid operations, the lawyers, soldiers and business men who had known him at the Club, and the wife of one of his oldest friends who had a special interest in common with him, for she is an expert gardener and grows world-famous camellias. All these men and women, and there were so many of them, made me realize how much he counted in their lives, and how difficult it must have been for him to leave Australia and come to work in England; and I gained a clearer idea than ever of our indebtedness to him for accepting the invitation to join the staff of our hospital. But wherever he went he quickly made friends, and there is no doubt that the welcome he received in London compensated to some extent for the separation from his older friends in Australia.

The high honours bestowed upon him indicate the esteem in which he was held by the Sovereign and by his professional brethren. His outstanding contributions to the practice of surgery and to medical literature are well known, and are recorded in their proper place. Though not unmindful of them now, I would prefer to lay stress upon the wonderful confidence he inspired in his patients, from the most lowly to the most exalted in the land, for every one of them felt sure that Sir Thomas had a full understanding of his or her individual problem, and that his wisdom and skill would be sufficient to deal with it. To inspire such confidence cost him tireless study and effort, anxiety and often loss of sleep, yet he never spared himself, and never relaxed until he had either won or lost the fight.

He set high standards for himself, and he insisted that those who assisted him, whether house surgeons or nurses or instrument makers, should comply with his instructions in minute detail. Other men have alienated the sympathy of their assistants by such tactics; but his associates discovered sooner or later that there was always reason and good reason behind his demands. Even the most expert had to acknowledge that they could learn from him; they all became his devoted slaves, and were rewarded by his approval, his friendship and even his love.

When training himself as a surgeon he studied the work of the masters; so also in the other interests and pursuits which made up his life he strove to learn from experts—in fishing, shooting and gardening; in the appreciation of pictures, furniture and architecture; and thus he became himself an expert. In literature he stuck to his old favourites, Shakespeare, Browning and George Meredith, and he read his Bible diligently and with more critical thought than many a regular churchgoer.

The last few years of his life were saddened (as is inevitable if a man lives beyond the allotted span) as one by one his old friends vanished away. And it would be selfish of us to think only of our own loss, and to be unmindful of the joy there must have been in heaven when Tom entered in.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR APRIL, 1958.

Courses for Higher Qualifications.

A course in microbiology, suitable for candidates for M.D., M.S. and post-graduate diplomas, will be held at the Bacteriology Department, University of Melbourne, at 2.15 p.m. on Tuesdays for about fifteen weeks, commencing on April 15. Enrolments, together with the fee of £9 9s., should be lodged with the Post-Graduate Committee by April 1.

A course in physics for D.D.R.I. and D.C.R.A.I. candidates will be held at the Commonwealth X-Ray and Radium Laboratory, Surrey Place, Melbourne, from 4 to 6 p.m. on Thursdays, commencing on April 10, for three or four months, provided there are sufficient candidates. Enrolments, together with the fee of £21, should be lodged with the Post-Graduate Committee by March 27.

Course in Ophthalmology.—Commencing on April 14, the Victorian Branch of the Ophthalmological Society of Australia will conduct a course in ophthalmic medicine and surgery and ocular pathology suitable for candidates for D.O. II, consisting of 70 to 80 lectures. These will be held in the late afternoon, chiefly on Tuesdays, Thursdays and Fridays, continuing till September. The fee for this course is £31 10s., and enrolments should be made through the Post-Graduate Committee on their special form by March 31.

In May, courses in psychiatry and radiodiagnosis will commence, and details will be announced shortly. Those wishing to attend a course in oto-rhino-laryngology and pathology, due to commence in June, should contact the Committee.

The honorary medical staff of Prince Henry's Hospital will conduct a course in medicine suitable for candidates for higher medical qualifications from May 26 for two months. Dr. M. D. Milne, of Hammersmith, will take part in the last four weeks of the course.

Refresher Course in General Medicine and Surgery.

A general refresher course will be conducted at Melbourne teaching hospitals, full time, from Monday, April 28, till Saturday, May 3. Two days will be spent at St. Vincent's Hospital studying medicine under the guidance of the medical staff, two days at the Alfred Hospital studying surgery under the guidance of the surgical staff, Wednesday morning at Fairfield Hospital, Wednesday afternoon at the Royal Children's Hospital, and Saturday morning at the Eye and Ear Hospital.

Enrolments, together with the fee of £9 9s., should be sent to the Post-Graduate Committee by April 14.

Arrangements will be made for lunch and parking of cars.

Course in Psychiatry.

The Department of Mental Hygiene will conduct a course in psychiatry on Tuesday evenings from 8 to 10 p.m. at the Royal Park Receiving House Training Centre, Oak Street. The course will be in two sections: from April 1 to May 27 a symposium on child psychiatry, and from June 3 to June 24 on general topics. There will also be various supplementary meetings.

All registered medical practitioners are invited to attend, without fee. Inquiries should be addressed to the Chief Clinical Officer, Mental Health Research Institute, Poplar Street, Royal Park, N.2.

Country Courses.

Sale.—On Saturday, April 12, at 2.30 p.m., there will be a clinical demonstration of gynaecological problems by Dr. J. W. Johnstone and Dr. Barry Kneale; at 4 p.m., a lecture by Dr. J. W. Johnstone, "Hormones in Gynaecology"; and at 8 p.m. a quiz session. The local secretary for this course is Dr. J. E. Joseph, 237 Princes Highway, Morwell. The fee for this course is £2 2s.¹

Warracknabeal.—On Saturday, April 12, in the hospital lecture room. The programme is as follows: 2.30 p.m., "The Coughing Child", Dr. M. L. Powell; 4.30 p.m., "Common Neurological Disorders", Dr. A. C. Schwieger; 8 p.m., "Cine-Pyelography and the Management of Hydronephrosis", Mr.

¹ Those who have paid an annual subscription to the Melbourne Post-Graduate Committee are invited to attend the above courses without further charge.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 1, 1958.¹

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	2(2)	8(2)	1	11
Amobiasis	..	1	3	1	..	1
Ancylostomiasis	4
Anthrax
Bilharziasis
Brucellosis	1	..	1	2
Cholera
Chorea (St. Vitus)	..	1(1)	1
Dengue
Diarrhoea (Infantile)	5(3)	15(15)	1	1	..	22
Diphtheria	1	2(2)	1(1)	4
Dysentery (Bacillary)	..	12(12)	4(4)	..	2(1)	18
Encephalitis	..	1(1)	1
Filariasis
Homologous Serum Jaundice
Hydatid
Infective Hepatitis	42(22)	10(11)	7(1)	9(6)	20(1)	1(1)	1	..	96
Lead Poisoning
Leprosy
Leptospirosis
Malaria	..	1(1)	1
Meningo-occal Infection	3(2)	1(1)	1(1)	..	1(1)	6
Ophthalmia
Ornithosis
Paratyphoid	1(1)	1
Plague
Poliomyelitis
Puerperal Fever
Rubella	..	20(15)	1(1)	11(10)	..	1	33
Salmonella Infection	1(1)	1(1)	2
Scarlet Fever	9(5)	21(17)	..	2	32
Smallpox
Tetanus	5(1)	2
Trachoma	16(9)	1	..	17
Trichinosis
Tuberculosis
Typhoid Fever	23(15)	18(14)	11(4)	20(17)	5(4)	5(4)	1	..	83
Typhus (Flea-, Mite- and Tick-borne)	1
Typhus (Louse-borne)
Yellow Fever

¹ Figures in parentheses are those for the metropolitan area.

J. Peters. The local secretary for this course is Dr. J. D. Searby, Warracknabeal. Fees are at the rate of 15s. per lecture.

Albury.—On Saturday and Sunday, April 19 and 20. The programme will include the following: "Aetiology and Treatment of Coronary Disease"; Professor J. G. Hayden: "Surgery of the Anus and Rectum"; Mr. E. S. R. Hughes: "Backache"; Mr. J. Cloke. Details of times and further sessions of this course will be announced shortly. The local secretary is Dr. Ross Hayter, Border Medical Association, 399 North Street, Albury. The course will be conducted in conjunction with the Sydney Post-Graduate Committee.

Flinders Naval Depot.

On Wednesday, April 9, at 2.30 p.m., Mr. Robert Kelly will talk on "Common Skin Diseases". This lecture will be given by arrangement with the Royal Australian Navy.

Overseas Lecturers.

Attention is directed to the visits of the following overseas lecturers during April:

Mr. John Blaikley, F.R.C.O.G., the Sims-Black Professor for 1958, will be in Melbourne from Tuesday, April 8, to Monday, April 14. On Wednesday, April 9, at 8.15 p.m., at Latrobe Street, he will give an open lecture to medical practitioners on "Recent Changes of Practice in Obstetrics". Further details may be obtained from the Victorian State Committee of the Royal College of Obstetricians and Gynaecologists.

Professor Saul Adler, O.B.E., M.R.C.P. (London), D.T.M. (Liverpool), F.R.S., Professor of Parasitology in the Hebrew University, Jerusalem, will give an open lecture on "Some Aspects of Drug Resistance" on Wednesday, April 16, at 8.15 p.m. at 8 Latrobe Street.

Professor Lucien Morris will visit Melbourne from April 23 to 27. Further details may be obtained from the Society of Anaesthetists.

Attention is directed to the visit of Professor M. L. Rosenheim, Sims Commonwealth Travelling Professor for 1958, who will be in Melbourne in May, and will deliver an open lecture to the medical profession at 8 p.m. on May 15 on "Chronic Pyelonephritis" in the B.M.A. Hall.

Preliminary Announcements.

Dr. M. D. Milne, M.D., M.R.C.P., physician and lecturer at the Post-Graduate Medical School, London, will visit Melbourne from June 26 to July 19 at the invitation of Prince Henry's Hospital.

Professor F. A. R. Stammers, Department of Surgery, Birmingham, will visit Melbourne from August 30 to September 13 as the Post-Graduate Committee's Category A Lecturer for 1958.

Professor Charles Illingworth has accepted the Committee's invitation to lecture, and will probably be in Melbourne for about a week from October 6.

Information.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne. Telephone: FB 2547.

The Royal Australasian College of Physicians.

VISIT OF PROFESSOR M. L. ROSENHEIM.

PROFESSOR M. L. ROSENHEIM, C.B.E., M.A. (Cambridge), M.D. (Cambridge), F.R.C.P., Sims Commonwealth Travelling Professor for 1958, will visit Sydney from Saturday, March 22, to Saturday, April 12, 1958. His programme will include visits to the teaching hospitals as follows: Sydney Hospital, March 25, 26 and 27; Royal Prince Alfred Hospital, March 27, 28 and 31; St. Vincent's Hospital, April 1, 2 and 3; Royal North Shore Hospital, April 8, 9 and 10; Royal Alexandra Hospital for Children, April 11.

Professor Rosenheim will address combined meetings of The Royal Australasian College of Physicians and the Royal Australasian College of Surgeons in the Stawell Hall as follows: Wednesday, March 26, at 5 p.m., "Unilateral Renal Disease and Hypertension"; Wednesday, April 2, at 8.15 p.m., "Cystinuria".

All members of the medical profession are invited to be present at a lecture to be given in the Stawell Hall in con-

junction with the Post-Graduate Committee in Medicine in the University of Sydney on Wednesday, April 9, at 8.15 p.m. Professor Rosenheim's subject will be "Sensitivity Reactions to Drugs".

Dominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Miles, Peter James, M.B., B.S., 1953 (Univ. Sydney), 31 Mepunga Street, Concord West, New South Wales.

Diary for the Month.

MARCH 25.—New South Wales Branch, B.M.A.: Council Quarterly.

MARCH 26.—Victorian Branch, B.M.A.: Council Meeting.

MARCH 27.—South Australian Branch, B.M.A.: Clinical Meeting.

MARCH 27.—New South Wales Branch, B.M.A.: Annual Meeting.

MARCH 28.—Queensland Branch, B.M.A.: Council Meeting.

MARCH 29.—Tasmanian Branch, B.M.A.: Annual Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales. Anti-Tuberculosis Association of New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or triple spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 per annum within Australia and the British Commonwealth of Nations, and £6 per annum within America and foreign countries, payable in advance.